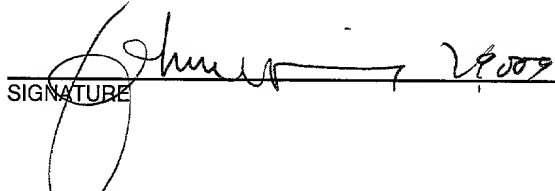


FORM PTO-1390 (REV 11-2000)	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY DOCKET NUMBER 468-30
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.5) 09/914286 Unknown
INTERNATIONAL APPLICATION NO. PCT/JP00/01041	INTERNATIONAL FILING DATE 23 February 2000	PRIORITY DATE CLAIMED 24 February 1999
TITLE OF INVENTION AVERMECTIN AGLYCON SYNTHASE GENES		
APPLICANT(S) FOR DO/EO/US OMURA et al.		
<p>Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:</p> <ol style="list-style-type: none"> <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. 371. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. <input checked="" type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below. <input checked="" type="checkbox"/> The U.S. has been elected by the expiration of 19 months from the priority date (Article 31). A copy of the International Application as filed (35 U.S.C. 371(c)(2)). <ol style="list-style-type: none"> <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau). <input checked="" type="checkbox"/> has been communicated by the International Bureau. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). <input checked="" type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)). <ol style="list-style-type: none"> <input checked="" type="checkbox"/> is attached hereto. <input type="checkbox"/> has been previously submitted under 35 U.S.C. 154(d)(4). <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)). <ol style="list-style-type: none"> <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau). <input type="checkbox"/> have been communicated by the International Bureau. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. <input type="checkbox"/> have not been made and will not be made. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). <input type="checkbox"/> A English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)). <p>Items 11 To 20 below concern document(s) or information included:</p> <ol style="list-style-type: none"> <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 C.F.R. 1.97 and 1.98. <input checked="" type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 C.F.R. 3.28 and 3.31 is included. <input type="checkbox"/> A FIRST preliminary amendment. <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment. <input type="checkbox"/> A substitute specification. <input type="checkbox"/> A change of power of attorney and/or address letter. <input type="checkbox"/> A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821-1.825. <input type="checkbox"/> A second copy of the published international application under 35 U.S.C. 154(d)(4). <input type="checkbox"/> A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4). <input checked="" type="checkbox"/> Other items or information. Sequence Listing (245 pages) / Front page of the PCT Publication 		

U.S. APPLICATION NO. (if known, see 37 C.F.R. 1.5) 09/914286		INTERNATIONAL APPLICATION NO. PCT/JP00/01041		ATTORNEY'S DOCKET NUMBER 468-30	
21. <input checked="" type="checkbox"/> The following fees are submitted:				CALCULATIONS PTO USE ONLY	
BASIC NATIONAL FEE (37 C.F.R. 1.492(a)(1)-(5): -- Neither international preliminary examination fee (37 C.F.R. 1.482) nor international search fee (37 C.F.R. 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO.....\$1000.00 -- International preliminary examination fee (37 C.F.R. 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO.....\$860.00 -- International preliminary examination fee (37 C.F.R. 1.482) not paid to USPTO but international search fee (37 C.F.R. 1.445(a)(2)) paid to USPTO.....\$710.00 -- International preliminary examination fee (37 C.F.R. 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4).....\$690.00 -- International preliminary examination fee (37 C.F.R. 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4).....\$100.00 <div style="text-align: right;">ENTER APPROPRIATE BASIC FEE AMOUNT =</div>				<div style="text-align: right;">\$ 860.00</div>	
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 C.F.R. 1.492(e)).				<div style="text-align: right;">\$ 0.00</div>	
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total Claims	57	-20 =	37	X	\$ 18.00
Independent Claims	17	-3 =	14	X	\$ 80.00
MULTIPLE DEPENDENT CLAIMS(S) (if applicable)					\$ 270.00
TOTAL OF ABOVE CALCULATIONS =					\$ 2916.00
<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.					0.00
SUBTOTAL =					\$ 2916.00
Processing fee of \$130.00, for furnishing the English Translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 C.F.R. 1.492(f)).					0.00
TOTAL NATIONAL FEE =					\$ 2916.00
Fee for recording the enclosed assignment (37 C.F.R. 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 C.F.R. 3.28, 3.31). \$40.00 per property					\$ 40.00
Fee for Petition to Revive Unintentionally Abandoned Application (\$1240.00 - Small Entity = \$620.00)					\$ 0.00
TOTAL FEES ENCLOSED =					\$ 2956.00
				Amount to be:	
				refunded	\$
				Charged	\$
a. <input checked="" type="checkbox"/> A check in the amount of \$2956.00 to cover the above fees is enclosed. b. <input type="checkbox"/> Please charge my Deposit Account No. 14-1140 in the amount of \$_____ to cover the above fees. A duplicate copy of this form is enclosed. c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-1140. A duplicate copy of this form is enclosed. d. <input checked="" type="checkbox"/> The entire content of the foreign application(s), referred to in this application is/are hereby incorporated by reference in this application.					
NOTE: Where an appropriate time limit under 37 C.F.R. 1.494 or 1.495 has not been met, a petition to revive (37 C.F.R. 1.137(a) or (b)) must be filed and granted to restore the application to pending status.					
SEND ALL CORRESPONDENCE TO: NIXON & VANDERHYE P.C. 1100 North Glebe Road, 8 th Floor Arlington, Virginia 22201-4714 Telephone: (703) 816-4000					
				SIGNATURE	
				 Arthur R. Crawford NAME	
				25,327	August 24, 2001
				REGISTRATION NUMBER	Date



PCT/PTO 07 DEC 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

OMURA et al.

Appln. No. 09/914,286

Filed: August 24, 2001

FOR: AVERMECTIN AGLYCON SYNTHASE GENES

Atty. Ref.: 468-30

Group Art Unit: Not Known

Examiner: Not Known

* * *

PRELIMINARY AMENDMENT AND SUBMISSION OF SEQUENCE LISTING

December 7, 2001

Hon. Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Notification of Missing Requirements mailed October 9, 2001, entry of the following amendments and remarks is respectfully requested.

IN THE SPECIFICATION

Kindly enter the following new paragraph.

Page 1, insert as the first paragraph following the title,

This is a national stage application under 35 U.S.C. 371 of PCT/JP00/01041, filed on February 23, 2000, now abandoned.

The specification is amended as follows.

Page 8, first paragraph starting on line 1,

(12) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity.

Page 11, fifth paragraph starting on line 29 and continuing to page 12,

(26) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705, and 25810-27102 of SEQ ID NO: 2; or
a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity.

Page 13, fourth paragraph starting on line 21 and continuing to page 14,

(33) A polypeptide comprising the amino acid sequence selected from the group consisting of amino acid Nos. 29-344, 366-451, 481-914, 1050-1356, 1715-1892, 1979-2060, 2086-2515, 2983-3128, 3537-3714 and 3805-3886 of SEQ ID NO: 3, amino acid Nos. 36-466, 596-908, 978-1059, 1083-1512, 1653-1964, 2306-2483, 2575-2656, 2680-3109, 3230-3538, 3878-4056, 4159-4240, 4271-4703, 4815-5122, 5168-5307, 5753-5930 and 6032-6113 of SEQ ID NO: 4, amino acid Nos. 34-461, 550-891, 1212-1396, 1483-1564, 1591-2020, 2108-2448, 2525-2606, 2636-3086, 3226-3591, 3629-3763, 4183-4363, 4460-4553 and 4627-4873 of SEQ ID NO: 5, amino acid Nos. 38-467, 574-914, 956-1081, 1488-1673, 1756-1837, 1864-2294, 2390-2732, 2776-2902, 3288-3473, 3556-3637, 3663-4093, 4182-4523, 4565-4685, 5085-5270 and 5353-5434 of SEQ ID NO: 6; or
a polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added in the amino acid sequence selected above, and having avermectin aglycon synthase domain activity.

Page 24, fourth paragraph starting on line 25 and continuing to page 25,
in SEQ ID NO: 4,
KS3: 36 to 466,
AT3: 596 to 908,
ACP3: 978 to 1059,
KS4: 1083 to 1512,
AT4: 1653 to 1964,
KR4: 2306 to 2483,
ACP4: 2575 to 2656,
KS5: 2680 to 3109,
AT5: 3230 to 3538,
KR5: 3878 to 4056,
ACP5: 4159 to 4240,
KS6: 4271 to 4703,
AT6: 4815 to 5122,
DH6: 5168 to 5307
KR6: 5753 to 5930,
ACP6: 6032 to 6113;

Page 26, third paragraph starting on line 21,

In other words, based on the above module, domain and ORF information obtained from DNAs having nucleotide sequences of SEQ ID NO: 1 and 2 derived from *Streptomyces avermitilis*, modules, domains and ORFs, which are relevant to the Avermectin aglycon synthase genes derived from other bacteria capable of producing avermectin, can be determined.

Page 35, first paragraph starting on line 1,

Specific examples include SP2/O, NSO and the like for mouse myeloma cells, YB2/O and the like for rat myeloma cells, HEK293 (ATCC: CRL-1573) and the like for

human fetal kidney cells, BALL-1 and the like for human leukemia cells, and COS-1, COS-7 and the like for African green monkey kidney cells.

Page 43, fifth paragraph starting on line 22,

Examples of the thus obtained protein include a protein comprising the amino acid sequences represented by SEQ ID NOS:3, 4, 5 and 6.

Page 43, sixth paragraph starting on line 25 and continuing to page 44,

Furthermore, a fusion protein of the protein of the present invention and other protein may be produced, and purified by affinity chromatography using a substance having affinity to the fusion protein. For example, the protein of the present invention may be produced as a fusion protein with protein A according to the method of Lowe *et al.* (*Proc. Natl. Acad. Sci. USA*, 86: 8227 (1989); *Genes Develop.*, 4: 1288 (1990)), or the method described in Japanese Published Unexamined Patent Application No. 336963/93 or WO 94/23021, and purified by affinity chromatography using immunoglobulin G.

IN THE CLAIMS

Kindly enter the following amended claims.

12. (Amended) The DNA according to claim 4 wherein the DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity is:
a DNA comprising comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of SEQ ID NO: 2; or
a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity.

26. (Amended) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297, and 24781-26079 of SEQ ID NO: 1 and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity

33. (Amended) A polypeptide comprising the amino acid sequence selected from the group consisting of amino acid Nos. 29-344, 366-451, 481-914, 1050-1356, 1715-1892, 1979-2060, 2086-2515, 2983-3128, 3537-3714 and 3805-3886 of SEQ ID NO: 3, amino acid Nos. 36-466, 596-908, 978-1059, 1083-1512, 1653-1964, 2306-2483, 2575-2656, 2680-3109, 3230-3538, 3878-4056, 4159-4240, 4271-4703, 4815-5122, 5168-5307, 5753-5930 and 6032-6113 of SEQ ID NO: 4, amino acid Nos. 34-461, 550-891, 1212-1396, 1483-1564, 1591-2020, 2108-2448, 2525-2606, 2636-3086, 3226-3591, 3629-3763, 4183-4363, 4460-4553 and 4627-4873 of SEQ ID NO: 5, amino acid Nos. 38-467, 574-914, 956-1081, 1488-1673, 1756-1837, 1864-2294, 2390-2732, 2776-2902, 3288-3473, 3556-3637, 3663-4093, 4182-4523, 4565-4685, 5085-5270 and 5353-5434 of SEQ ID NO: 6; or

a polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added in the amino acid sequence selected above, and having avermectin aglycon synthase domain activity.

IN THE SEQUENCE LISTING

Kindly enter the attached substitute paper and computer readable forms of the Sequence Listing in lieu of the Sequence Listing submitted on August 24, 2001.

REMARKS

Claims 1-43 are pending.

Substitute paper and original computer readable forms of the Sequence Listing are being submitted herewith in response to the requirement under 35 U.S.C. 371 to comply with the Sequence Rules 37 CFR § 1.821 et seq. The attached substitute paper and original computer readable forms of the Sequence Listing do not add new matter, and their contents are the same. Typographical errors in the length of SEQ ID NOS:1 and 7 have been corrected. Prompt notice of any defects in the Sequence Listing is earnestly solicited and additional time is requested to comply.

A statement claiming priority under 35 U.S.C. 371 is added after the title. Furthermore, errors in the specification are being corrected.

Applicants earnestly solicit an early examination on the merits. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By:



Gary R. Tanigawa
Reg. No. 43,180

1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

APPENDIX

MARKED-UP VERSION TO SHOW CHANGES

IN THE SPECIFICATION

The following new paragraph is added on page 1 after the title:

This is a national stage application under 35 U.S.C. 371 of PCT/JP00/01041, filed on February 23, 2000, now abandoned.

The specification is amended as follows.

Page 8, first paragraph starting on line 1,

(12) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity is:
a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of [SEQ ID NO:1] SEQ ID NO: 2; or
a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity.

Page 11, fifth paragraph starting on line 29 and continuing to page 12,

(26) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705, and 25810-27102 of [SEQ ID NO: 1] SEQ ID NO: 2; or
a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity.

Page 13, fourth paragraph starting on line 21 and continuing to page 14,

(33) A polypeptide comprising the amino acid sequence selected from the group consisting of amino acid Nos. 29-344, 366-451, 481-914, 1050-1356, 1715-1892, 1979-2060, 2086-2515, 2983-3128, 3537-3714 and 3805-3886 of SEQ ID NO: 3, amino acid Nos. 36-466, 596-908, 978-1059, 1083-1512, 1653-1964, 2306-2483, 2575-2656, 2680-3109, [32030-3538] 3230-3538, 3878-4056, 4159-4240, 4271-4703, 4815-5122, 5168-5307, 5753-5930 and 6032-6113 of SEQ ID NO: 4, amino acid Nos. 34-461, 550-891, 1212-1396, 1483-1564, 1591-2020, 2108-2448, 2525-2606, 2636-3086, 3226-3591, 3629-3763, 4183-4363, 4460-4553 and 4627-4873 of SEQ ID NO: 5, amino acid Nos. 38-467, 574-914, 956-1081, 1488-1673, 1756-1837, 1864-2294, 2390-2732, 2776-2902, 3288-3473, 3556-3637, 3663-4093, 4182-4523, 4565-4685, 5085-5270 and 5353-5434 of SEQ ID NO: 6; or
a polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added in the amino acid sequence selected above, and having avermectin aglycon synthase domain activity.

Page 24, fourth paragraph starting on line 25 and continuing to page 25,
in SEQ ID NO: 4,

KS3: 36 to 466,

AT3: 596 to 908,

ACP3: 978 to 1059,

KS4: 1083 to 1512,

AT4: 1653 to 1964,

KR4: 2306 to 2483,

ACP4: 2575 to 2656,

KS5: 2680 to 3109,

AT5: [32030 to 3538] 3230 to 3538,

KR5: 3878 to 4056,

ACP5: 4159 to 4240,

KS6: 4271 to 4703,

AT6: 4815 to 5122,

DH6: 5168 to 5307

[DH6: 5753 to 5930] KR6: 5753 to 5930,

ACP6: 6032 to 6113;

Page 26, third paragraph starting on line 21,

In other words, based on the above module, domain and ORF information obtained from DNAs having nucleotide sequences of SEQ ID NO: 1 and 2 derived from *Streptomyces avermitilis*, modules, domains and ORFs, which are relevant to the Avermectin aglycon synthase genes [of the present invention] derived from other bacteria capable of producing avermectin, can be determined.

Page 35, first paragraph starting on line 1,

Specific examples include SP2/O, NSO and the like for mouse myeloma cells, YB2/O and the like for rat myeloma cells, HEK293 (ATCC: CRL-1573)[, 293] and the like for human fetal kidney cells, BALL-1 and the like for human leukemia cells, and COS-1, COS-7 and the like for African green monkey kidney cells.

Page 43, fifth paragraph starting on line 22,

Examples of the thus obtained protein include a protein comprising [the amino acid sequence represented by SEQ ID NO:1] the amino acid sequences represented by SEQ ID NOS:3, 4, 5 and 6.

Page 43, sixth paragraph starting on line 25 and continuing to page 44,

Furthermore, a fusion protein of the protein of the present invention and other protein may be produced, and purified by affinity chromatography using a substance having affinity to the fusion protein. For example, the protein of the present invention may be produced as a fusion protein with protein A according to the method of Lowe *et al.* (*Proc. Natl. Acad. Sci. USA*, 86: 8227 (1989); *Genes Develop.*, 4: 1288 (1990)), or the method described in Japanese Published Unexamined Patent Application No.

336963/93 or [823021/94] WO 94/23021, and purified by affinity chromatography using immunoglobulin G.

IN THE CLAIMS

The claims are amended as follows.

12. (Amended) The DNA according to claim 4 wherein the DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity is:
a DNA comprising comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of [SEQ ID NO: 1] SEQ ID NO: 2; or
a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity.

26. (Amended) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297, and 24781-26079 of SEQ ID NO: 1 and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of [SEQ ID NO: 1] SEQ ID NO: 2; or
a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity

33. (Amended) A polypeptide comprising the amino acid sequence selected from the group consisting of amino acid Nos. 29-344, 366-451, 481-914, 1050-1356, 1715-1892, 1979-2060, 2086-2515, 2983-3128, 3537-3714 and 3805-3886 of SEQ ID NO: 3, amino acid Nos. 36-466, 596-908, 978-1059, 1083-1512, 1653-1964, 2306-2483, 2575-2656, 2680-3109, [32030-3538] 3230-3538, 3878-4056, 4159-4240, 4271-4703, 4815-5122, 5168-5307, 5753-5930 and 6032-6113 of SEQ ID NO: 4, amino acid

Nos. 34-461, 550-891, 1212-1396, 1483-1564, 1591-2020, 2108-2448, 2525-2606, 2636-3086, 3226-3591, 3629-3763, 4183-4363, 4460-4553 and 4627-4873 of SEQ ID NO: 5, amino acid Nos. 38-467, 574-914, 956-1081, 1488-1673, 1756-1837, 1864-2294, 2390-2732, 2776-2902, 3288-3473, 3556-3637, 3663-4093, 4182-4523, 4565-4685, 5085-5270 and 5353-5434 of SEQ ID NO: 6; or
a polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added in the amino acid sequence selected above, and having avermectin aglycon synthase domain activity.

IN THE SEQUENCE LISTING

The substitute paper and original computer readable forms of the Sequence Listing are attached.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

Atty Dkt. 462-30

Rec'd PCT/PTO 07 DEC 2001

OMURA et al.

C# M#

Group Art Unit: Not Known

Appln. No. 09/914,286

Examiner: Not Known

Filed: August 24, 2001

Date: December 7, 2001

Title: AVERMECTIN AGLYCON PHASE GENES

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

PRELIMINARY AMENDMENT AND SUBMISSION OF SEQUENCE LISTING

This is a response/amendment/letter in the above-identified application and includes an attachment which is hereby incorporated by reference and the signature below serves as the signature to the attachment in the absence of any other signature thereon.

Fees are attached as calculated below:

Total effective claims after amendment **57** minus highest number
previously paid for **57** (at least 20) = 0 x \$ 0.00

Independent claims after amendment **17** minus highest number
previously paid for **17** (at least 3) = 0 x \$ 0.00

If proper multiple dependent claims now added for first time, add \$ (ignore improper) \$ 0.00

Extension is hereby made to extend the current due date so as to cover the filing date of this
paper and attachment(s) (\$ /1 month; \$ /2 months; \$ /3 months) \$ 0.00

Terminal disclaimer enclosed, add \$ \$ 0.00

☐ First/second submission after Final Rejection pursuant to 37 CFR 1.129(a) (\$) \$ 0.00

☐ Please enter the previously unentered, filed

☐ Submission attached

Subtotal \$ 0.00

If "small entity," then enter half (1/2) of subtotal and subtract -\$ 0.00

☐ Applicant claims "small entity" status. ☐ Statement filed herewith

Rule 56 Information Disclosure Statement Filing Fee (\$) \$ 0.00

Assignment Recording Fee (\$) \$ 0.00

Other: **PAPER COPY OF SEQUENCE LISTING AND FLOPPY DISK IN COMPUTER READABLE FORM 0.00**

TOTAL FEE ENCLOSED \$ 0.00

The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Account No. 14-1140. A duplicate copy of this sheet is attached.

1100 North Glebe Road, 8th Floor
Arlington, Virginia 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100
GRT:ap

NIXON & VANDERHYE P.C.
By Atty: Gary R. Tanigawa, Reg. No. 43,180

Signature: 

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

Atty Dkt. 468-30

C# M#

OMURA et al.

Group Art Unit: Not Known

Appln. No. 09/914,286

Examiner: Not Known

Filed: August 24, 2001

Date: December 7, 2001

Title: AVERMECTIN AGLYCON SYNTHASE GENES

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

PRELIMINARY AMENDMENT AND SUBMISSION OF SEQUENCE LISTING

This is a response/amendment/letter in the above-identified application and includes an attachment which is hereby incorporated by reference and the signature below serves as the signature to the attachment in the absence of any other signature thereon.

Fees are attached as calculated below:

Total effective claims after amendment **57** minus highest number
previously paid for **57** (at least 20) = 0 x \$ 0.00

Independent claims after amendment **17** minus highest number
previously paid for **17** (at least 3) = 0 x \$ 0.00

If proper multiple dependent claims now added for first time, add \$ (ignore improper) \$ 0.00

Petition is hereby made to extend the current due date so as to cover the filing date of this
paper and attachment(s) (\$ /1 month; \$ /2 months; \$ /3 months) \$ 0.00

Terminal disclaimer enclosed, add \$ \$ 0.00

☐ First/second submission after Final Rejection pursuant to 37 CFR 1.129(a) (\$) \$ 0.00

☐ Please enter the previously unentered, filed

☐ Submission attached

Subtotal \$ 0.00

If "small entity," then enter half (1/2) of subtotal and subtract -\$ 0.00

☐ Applicant claims "small entity" status. ☐ Statement filed herewith

Rule 56 Information Disclosure Statement Filing Fee (\$) \$ 0.00

Assignment Recording Fee (\$) \$ 0.00

Other: **PAPER COPY OF SEQUENCE LISTING AND FLOPPY DISK IN COMPUTER READABLE FORM 0.00**

TOTAL FEE ENCLOSED \$ 0.00

The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Account No. 14-1140. A duplicate copy of this sheet is attached.

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NIXON & VANDERHYTE P.C.

By Atty: Gary R. Tanigawa, Reg. No. 43,180

Signature: 



SEQUENCE LISTING

<110> OMURA, Satoshi
IKEDA, Haruo

<120> AVERMECTIN AGLYCON SYNTHASE GENES

<130> 468-30/PH-775-PCT

<140> US 09/914,286

<141> 2001-08-24

<150> PCT/JP00/01041

<151> 2000-02-23

<150> JP 99/46961

<151> 1999-02-24

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<170> PatentIn Ver. 2.0

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Thr Ser Asn Pro Asp Gln Leu Gln Gln Leu Leu Asn Thr Ile Pro Pro	
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caa cac ccc ctc acc acc gtc atc cac acc gca ggc atc ctc gac gac	5424
Gln His Pro Leu Thr Thr Val Ile His Thr Ala Gly Ile Leu Asp Asp	
1795 1800 1805	
gcc acc ctc acc aac ctc acc ccc acc caa ctc aac aac gtc ctc cgc	5472
Ala Thr Leu Thr Asn Leu Thr Pro Thr Gln Leu Asn Asn Val Leu Arg	
1810 1815 1820	
gcc aaa gcc cac agc gcc cac ctc ctc cac caa ctc acc caa cac acc	5520
Ala Lys Ala His Ser Ala His Leu Leu His Gln Leu Thr Gln His Thr	
1825 1830 1835 1840	
ccc ctc acc gcc ttc gtc ctc tac tcc tcc gcc gcc gcc acc ttc ggc	5568
Pro Leu Thr Ala Phe Val Leu Tyr Ser Ser Ala Ala Ala Thr Phe Gly	
1845 1850 1855	
gca ccc ggc caa gcc aac tac gcc gca gcc aac gcc tac ctc gac gcc	5616
Ala Pro Gly Gln Ala Asn Tyr Ala Ala Ala Asn Ala Tyr Leu Asp Ala	
1860 1865 1870	
ctc gcc cac cac cgc cac acc cac cac ctc ccc gcc acc agc atc gcc	5664
Leu Ala His His Arg His Thr His His Leu Pro Ala Thr Ser Ile Ala	
1875 1880 1885	
tgg ggc acc tgg caa gga aac gga ctc gct gat tcg gac aag gcc cgc	5712
Trp Gly Thr Trp Gln Gly Asn Gly Leu Ala Asp Ser Asp Lys Ala Arg	
1890 1895 1900	
gca tat ctc gac cgc cgc ggg ttt cga ccc atg tca ccc gag ttg gcc	5760
Ala Tyr Leu Asp Arg Arg Gly Phe Arg Pro Met Ser Pro Glu Leu Ala	
1905 1910 1915 1920	
acg gca gcg gtc acg cag gcg atc gcg gac acc gaa cgg ccg tat gtc	5808
Thr Ala Ala Val Thr Gln Ala Ile Ala Asp Thr Glu Arg Pro Tyr Val	
1925 1930 1935	
gtc atc gcc gac atc gac tgg agc aag atc gaa cac acc tct cag acc	5856
Val Ile Ala Asp Ile Asp Trp Ser Lys Ile Glu His Thr Ser Gln Thr	
1940 1945 1950	
agc gac ctg gtg agc gcg gcc cgg gaa agg gag cca gct gtc cag cgc	5904
Ser Asp Leu Val Ser Ala Ala Arg Glu Arg Glu Pro Ala Val Gln Arg	
1955 1960 1965	
ccc act cca ccg gcg gag ttg cac aaa acg ctg gcc cat cag acg tcg	5952
Pro Thr Pro Pro Ala Glu Leu His Lys Thr Leu Ala His Gln Thr Ser	
1970 1975 1980	
gcc gac caa cgg gcc gca ttg ctc gag ctc gta cga gac cat gtg gcg	6000
Ala Asp Gln Arg Ala Ala Leu Leu Glu Leu Val Arg Asp His Val Ala	
1985 1990 1995 2000	
gca gtg ctc cgg cac gcg gac ccg aaa gcc atc gcg ccc gac cag tcg	6048
Ala Val Leu Arg His Ala Asp Pro Lys Ala Ile Ala Pro Asp Gln Ser	
2005 2010 2015	

ttc cgt gca ctc ggc ttc gat tca ctc acg gcc gtc gag ttc cga aac Phe Arg Ala Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Phe Arg Asn 2020 2025 2030	6096
ctg ctg atc aag gca aca gga ctc cgc ctt cct gtc tcg ctg gtc ttc Leu Leu Ile Lys Ala Thr Gly Leu Arg Leu Pro Val Ser Leu Val Phe 2035 2040 2045	6144
gac cac ccg acc cct gcc aaa ctc gcc gta cac ctg cag aac caa ctg Asp His Pro Thr Pro Ala Lys Leu Ala Val His Leu Gln Asn Gln Leu 2050 2055 2060	6192
cgg ggc aca gca gcg gag tcg gct cct tca gcg gca gcc gtt acc gcc Arg Gly Thr Ala Ala Glu Ser Ala Pro Ser Ala Ala Val Thr Ala 2065 2070 2075 2080	6240
gag gct tct gtc acc gag ccg atc gcc atc gtt ggc atg gcc tgt cgt Glu Ala Ser Val Thr Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg 2085 2090 2095	6288
ttc ccc ggc gga gtg acc tcg gcg gac gac ttc tgg gat ctg atc tcc Phe Pro Gly Gly Val Thr Ser Ala Asp Phe Trp Asp Leu Ile Ser 2100 2105 2110	6336
tcc gag cag gac gcg atc ggc gga ttc ccc acc gac cgc ggc tgg gac Ser Glu Gln Asp Ala Ile Gly Gly Phe Pro Thr Asp Arg Gly Trp Asp 2115 2120 2125	6384
ctg gac acg ctc tac gac ccc gac ccc gac cac ccc ggc acc tgc tac Leu Asp Thr Leu Tyr Asp Pro Asp Pro Asp His Pro Gly Thr Cys Tyr 2130 2135 2140	6432
acc cga aac ggc gga ttc ctc tac gac gca ggc cac ttc gac gcc gaa Thr Arg Asn Gly Gly Phe Leu Tyr Asp Ala Gly His Phe Asp Ala Glu 2145 2150 2155 2160	6480
ttc ttc ggc atc agc ccc cgc gaa gcc ctc gcc atg gac ccc cag caa Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln 2165 2170 2175	6528
cga ctc ctc ctc gaa acc gcc tgg gaa acc atc gaa cac gcc ggc atc Arg Leu Leu Leu Glu Thr Ala Trp Glu Thr Ile Glu His Ala Gly Ile 2180 2185 2190	6576
aac ccc cac acc ctc cac ggc acc ccc acc gga gtc ttc acc ggc acc Asn Pro His Thr Leu His Gly Thr Pro Thr Gly Val Phe Thr Gly Thr 2195 2200 2205	6624
aac gga cag gac tac gca ctt cgc gtg cac aac gcg ggc cag tca acc Asn Gly Gln Asp Tyr Ala Leu Arg Val His Asn Ala Gly Gln Ser Thr 2210 2215 2220	6672
gat ggt ttc gca ctg acc gga acc gcc ggc agc gtc atc tcc ggt cgt Asp Gly Phe Ala Leu Thr Gly Thr Ala Gly Ser Val Ile Ser Gly Arg 2225 2230 2235 2240	6720
atc tcg tac acg ttt ggt ttt gag ggt cct gcg gtg tcg gtg gac acg Ile Ser Tyr Thr Phe Gly Phe Glu Gly Pro Ala Val Ser Val Asp Thr 2245 2250 2255	6768

gct tgt tcc tgc tgc ttg gtg gct ttg cat ctg gcc tgt cag gcg ttg	6816
Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala Leu	
2260 2265 2270	
cggt gcg ggt gag tgc tgc atg gcg ctt gcc ggg ggt gtg acg gtg atg	6864
Arg Ala Gly Glu Cys Ser Met Ala Leu Ala Gly Gly Val Thr Val Met	
2275 2280 2285	
tgc tct ccg ggt gcc ttc gtg gag ttt tgc cgg cag cgg ggt ctg gcc	6912
Ser Ser Pro Gly Ala Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala	
2290 2295 2300	
gcg gac ggg cat tgc aag gcg ttc tgc gcg gcg gcg gac ggg acc ggc	6960
Ala Asp Gly His Cys Lys Ala Phe Ser Ala Ala Ala Asp Gly Thr Gly	
2305 2310 2315 2320	
tgg ggt gag ggt gtg ggg atg ctg ctg gtg gag cgg ctc tcc gac gcc	7008
Trp Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala	
2325 2330 2335	
cat cgc aac ggt cac cgt gtc ctg gcc gtg gtg cgt ggc agt gcg gtc	7056
His Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val	
2340 2345 2350	
aac cag gac ggt gcg agc aac ggt ctg acc gcg ccc aac ggg ccg tcc	7104
Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser	
2355 2360 2365	
cag cag cgt gtc atc cgc cag gcc ctc gcc aac gcc ggc ttg tgc gcc	7152
Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Ser Ala	
2370 2375 2380	
ggt gat gtc gac gcg gtg gag gcc cac ggc acc ggc acc act ttg ggc	7200
Gly Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Thr Leu Gly	
2385 2390 2395 2400	
gac ccg atc gag gcc cag gcc ctc ctc gcg acc tac gga cag gac cgt	7248
Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Asp Arg	
2405 2410 2415	
gcc ggc gag ggg ccg ctg tgg ctg ggc tgc gtc aag tcc aat gtc ggt	7296
Ala Gly Glu Gly Pro Leu Trp Leu Gly Ser Val Lys Ser Asn Val Gly	
2420 2425 2430	
cac aca cag gct gcc gcg ggc gtc gcc ggg gtg atc aag atg gtg atg	7344
His Thr Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val Met	
2435 2440 2445	
gcg ctg ccg cat ggt ctg ctg ccg cgg acg ttg cat gtg gat gag ccg	7392
Ala Leu Arg His Gly Leu Leu Pro Arg Thr Leu His Val Asp Glu Pro	
2450 2455 2460	
tgc ccg cat gtg gac tgg tcc gcg ggt gcg gtg cag ctg ctg acg gag	7440
Ser Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu Leu Thr Glu	
2465 2470 2475 2480	
acg gtg ccc tgg ccc ggc ggg gag ggg cgg cta cgg cgg gca gga gtg	7488
Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Leu Arg Arg Ala Gly Val	
2485 2490 2495	

tca tca ttc ggc gtc agc ggc acc aac gcc cac gtc atc ctc gaa gaa	7536
Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu	
2500 2505 2510	
gca ccc gcc gac gac gtt ccg ggg gga cca ccc gcc ggc gag ggt gac	7584
Ala Pro Ala Asp Asp Val Pro Gly Gly Pro Pro Ala Gly Glu Gly Asp	
2515 2520 2525	
gcg ggc agc gac gat gag gct gct gcc ggc agt cct ggg gtg tgg ccg	7632
Ala Gly Ser Asp Asp Glu Ala Ala Ala Gly Ser Pro Gly Val Trp Pro	
2530 2535 2540	
tgg ctg gtg tgc gcc aag tgc cag ccg gcc ctg cgc gcc cag gcc cag	7680
Trp Leu Val Ser Ala Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln	
2545 2550 2555 2560	
gcc ctg cac gcc cac ctc acc gac cac ccc ggc ctc gac ctc gcg gat	7728
Ala Leu His Ala His Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp	
2565 2570 2575	
gtc gga tac acc ctc gcc cac gcc cgc gcc gtg ttc gac cac cgc gcc	7776
Val Gly Tyr Thr Leu Ala His Ala Arg Ala Val Phe Asp His Arg Ala	
2580 2585 2590	
acc ctc atc gcc gcg gac cgc gac acg ttc ctg caa gca ctc cag gca	7824
Thr Leu Ile Ala Ala Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala	
2595 2600 2605	
ctc gcc gca ggc gag ccc cac ccc gcc gtc atc cac agc agc gcc ccg	7872
Leu Ala Ala Gly Glu Pro His Pro Ala Val Ile His Ser Ser Ala Pro	
2610 2615 2620	
ggc ggg acc ggg acc ggg gag gcc gca gga aag acc gca ttc atc tgc	7920
Gly Gly Thr Gly Thr Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys	
2625 2630 2635 2640	
tcc gga cag ggc acc caa cgc ccc ggc atg gcc cac ggc ctc tac cac	7968
Ser Gly Gln Gly Thr Gln Arg Pro Gly Met Ala His Gly Leu Tyr His	
2645 2650 2655	
acc cac ccc gtc ttc gcc gcc gca ctc aac gac atc tgc acc cac ctc	8016
Thr His Pro Val Phe Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu	
2660 2665 2670	
gac ccc cac ctc gac cac ccc ctc ctc ccc ctc ctc acc caa aac gac	8064
Asp Pro His Leu Asp His Pro Leu Leu Pro Leu Leu Thr Gln Asn Asp	
2675 2680 2685	
aac gac aac gag gac gcg gcc gca ctg ctc cag cag acc cgc tac gcc	8112
Asn Asp Asn Glu Asp Ala Ala Ala Leu Leu Gln Gln Thr Arg Tyr Ala	
2690 2695 2700	
cag ccc gcc ctc ttc gcc ttc cag gtc gcc ctc cac cgc ctc ctc acc	8160
Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr	
2705 2710 2715 2720	
gac ggc tac cac atc acc ccc cac tac tac gcc gga cac tcc ctc ggc	8208
Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly	
2725 2730 2735	

gaa atc acc gcc gcc cac ctc gcc ggc atc ctc acc ctc acc gac gcc	8256
Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala	
2740 2745 2750	
acc acc ctc atc acc caa cgc gcc acc ctc atg caa acc atg ccc ccc	8304
Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro	
2755 2760 2765	
ggc acc atg acc acc ctc cac acc acc ccc cac cac atc acc cac cac	8352
Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His His	
2770 2775 2780	
ctc acc gcc cac gaa aac gac ctc gcc atc gcc gcc atc aac acc ccc	8400
Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro	
2785 2790 2795 2800	
acc tcc ctc gtc atc agc ggc acc ccc cac acc gtc caa cac atc acc	8448
Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr	
2805 2810 2815	
acc ctc tgc caa caa caa ggc atc aaa acc aaa acc ctc ccc acc aac	8496
Thr Leu Cys Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Asn	
2820 2825 2830	
cac gcc ttc cac tcc ccc cac acc aac ccc atc ctc aac caa ctc cac	8544
His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His	
2835 2840 2845	
cag cac acc caa acc ctc acc tac cac cca ccc cac acc ccc ctc atc	8592
Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile	
2850 2855 2860	
acc gcc aac acc cca ccc gac caa ctc ctc acc ccc cac tac tgg acc	8640
Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr	
2865 2870 2875 2880	
caa caa gcc cgc aac acc gtc gac tac gcc acc acc acc caa acc ctc	8688
Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr Leu	
2885 2890 2895	
cac caa cac ggc gtc acc acc tac atc gaa ctc gga ccc gac aac acc	8736
His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr	
2900 2905 2910	
ctc acc acc ctc acc cac cac aac ctc ccc aac ccc ccc acc acc acc	8784
Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Pro Pro Thr Thr Thr	
2915 2920 2925	
ctc acc ctc acc cac ccc cac cac cac ccc caa acc cac ctc ctc acc	8832
Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu Thr	
2930 2935 2940	
aac ctc gcc aaa acc acc acc acc tgg cac ccc cac cac tac acc cac	8880
Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr His	
2945 2950 2955 2960	
cac gac aac caa ccc cac acc cac acc cac ctc gac ctc ccc acc tac	8928
His Asp Asn Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr	
2965 2970 2975	

ccc ttc caa cac cac cac tac tgg ctc gaa agc aca cag ccc ggt gcc	8976
Pro Phe Gln His His His Tyr Trp Leu Glu Ser Thr Gln Pro Gly Ala	
2980 2985 2990	
ggc aac gtg tca gca gcc gga ctc gac ccc acc gaa cac ccc cta ctc	9024
Gly Asn Val Ser Ala Ala Gly Leu Asp Pro Thr Glu His Pro Leu Leu	
2995 3000 3005	
ggc gcc aca ttg gaa ctg gcg act gac ggt gga gcg ctt ctt gca ggg	9072
Gly Ala Thr Leu Glu Leu Ala Thr Asp Gly Gly Ala Leu Leu Ala Gly	
3010 3015 3020	
cgc ttg tct ttg agg tcg cat ccg tgg ctg gct gac cat gcc gtc ggc	9120
Arg Leu Ser Leu Arg Ser His Pro Trp Leu Ala Asp His Ala Val Gly	
3025 3030 3035 3040	
ggc acg gtg ctg ctg tcg ggc gcc acc ttc ctc gaa ctc gcc ctt cat	9168
Gly Thr Val Leu Leu Ser Gly Ala Thr Phe Leu Glu Leu Ala Leu His	
3045 3050 3055	
gcg ggc aca tac gtg ggc tgc gac cga gtg gat gag ctg acg ctg cat	9216
Ala Gly Thr Tyr Val Gly Cys Asp Arg Val Asp Glu Leu Thr Leu His	
3060 3065 3070	
gcg ccg ctg gtg gtt cct gtg gat ggg ggt gtg agt gtg cag gtt ggg	9264
Ala Pro Leu Val Val Pro Val Asp Gly Gly Val Ser Val Gln Val Gly	
3075 3080 3085	
gtt gcg gct gcg gat ggg gag ggg ccg cgt ttg gtg agt gtg tat gcg	9312
Val Ala Ala Ala Asp Gly Glu Gly Arg Arg Leu Val Ser Val Tyr Ala	
3090 3095 3100	
ccg ggt ggg agt gct tgt ggt ggg ggt ggt gcg tcg ggt ggg gtg tgg	9360
Arg Gly Gly Ser Ala Cys Gly Gly Gly Gly Ala Ser Gly Gly Val Trp	
3105 3110 3115 3120	
acg tgt cat gcc tcg ggg gtg ctg gtt gag gct gct gct ggt ggt gtg	9408
Thr Cys His Ala Ser Gly Val Leu Val Glu Ala Ala Ala Gly Gly Val	
3125 3130 3135	
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Val Val Asp Gly Leu Ala Gly Val Trp Pro Pro Arg Gly Ala Val Ala	
3140 3145 3150	
gtg gat gtc gat ggt gtc cgt gac cgt ttg gct ggg gct ggt tgt gtt	9504
Val Asp Val Asp Gly Val Arg Asp Arg Leu Ala Gly Ala Gly Cys Val	
3155 3160 3165	
ttg ggg ccg gtg ttt tcg ggg ctg cgt gcg gtg tgg cgt gat ggg ggg	9552
Leu Gly Pro Val Phe Ser Gly Leu Arg Ala Val Trp Arg Asp Gly Gly	
3170 3175 3180	
gat ttg ctg gct gag gtg tgt ctg ccg gag gag gcg tgg ggt gat gcg	9600
Asp Leu Leu Ala Glu Val Cys Leu Pro Glu Glu Ala Trp Gly Asp Ala	
3185 3190 3195 3200	
gct ggt ttt ggg ctg cat ccg gcg ttg ctg gat ggt gtg gtc cag ccg	9648
Ala Gly Phe Gly Leu His Pro Ala Leu Leu Asp Gly Val Val Gln Pro	
3205 3210 3215	

ttg tcg gtg ttg ctt ccg ggt ggg acg ggg ttt ggg gag ggg gcg ggg	9696
Leu Ser Val Leu Leu Pro Gly Gly Thr Gly Phe Gly Glu Gly Ala Gly	
3220 3225 3230	
ttc ggg gag ggt gtt ccg gtg ccg gct gtg tgg ggt ggt gtg tcg ctt	9744
Phe Gly Glu Gly Val Arg Val Pro Ala Val Trp Gly Gly Val Ser Leu	
3235 3240 3245	
cac ccg gcg ggt gtg acc ggt gtg ccg gtg cgt gtg tcg gct gtc ggg	9792
His Arg Ala Gly Val Thr Gly Val Arg Val Arg Val Ser Ala Val Gly	
3250 3255 3260	
ccg ggc ggc ggg cgt gag gcg gtg tcg gtc gtg gtc ggg gat gag gcg	9840
Arg Gly Gly Gly Arg Glu Ala Val Ser Val Val Val Gly Asp Glu Ala	
3265 3270 3275 3280	
ggt gtg ccg gtg gcg tcg gtc gat cgt ctt gag ttg ccg cct gtg gat	9888
Gly Val Pro Val Ala Ser Val Asp Arg Leu Glu Leu Arg Pro Val Asp	
3285 3290 3295	
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Met Gly Gln Leu Arg Ala Val Ser Val Ser Ala Gly Arg Arg Gly Ser	
3300 3305 3310	
ctg tat gcg gtg cag tgg gct gag gtg ggt cct gtg ccg gtg tgt ggg	9984
Leu Tyr Ala Val Gln Trp Ala Glu Val Gly Pro Val Pro Val Cys Gly	
3315 3320 3325	
cag gcg tgg gcg tgg cac gag gac gtg ggt gag agc ggt ggt ggg cct	10032
Gln Ala Trp Ala Trp His Glu Asp Val Gly Glu Ser Gly Gly Gly Pro	
3330 3335 3340	
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Val Pro Gly Val Val Val Leu Arg Cys Pro Asp Ala Gly Ala Gly Gly	
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Gly Gly Gly Gly Gly Gly Gly Gly Gly Val Gly Glu Val Val Gly Gly	
3365 3370 3375	
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Val Leu Gly Val Val Gln Gly Trp Leu Gly Leu Glu Arg Phe Ala Gly	
3380 3385 3390	
tcg ccg ctg gtg gtg gtg acc ccg ggt gcg gtg gtg gcc ggc ccg gag	10224
Ser Arg Leu Val Val Val Thr Arg Gly Ala Val Val Ala Gly Pro Glu	
3395 3400 3405	
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Asp Gly Pro Val Asp Val Val Gly Ala Ser Val Trp Gly Leu Val Arg	
3410 3415 3420	
tcg gcg cag gct gag cat ccg gac ccg ttt gtc ctc ctc gac ctc gac	10320
Ser Ala Gln Ala Glu His Pro Asp Arg Phe Val Leu Leu Asp Leu Asp	
3425 3430 3435 3440	
acc gac acc ggc acc gac ctc gac acc ggt gct ggt gct ggt tgg ggc	10368
Thr Asp Thr Gly Thr Asp Leu Asp Thr Gly Ala Gly Ala Gly Trp Gly	
3445 3450 3455	

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ttg gcg gtg cgt ggg gag cgg ttg ctg gcc gca cgc ctg aaa cga ctt Leu Ala Val Arg Gly Glu Arg Leu Leu Ala Ala Arg Leu Lys Arg Leu 3475 3480 3485	10464
gag tca tcc ggt gat gtt cca gcc cag cgg tcc ggt gac aca cga gcc Glu Ser Ser Gly Asp Val Pro Ala Gln Arg Ser Gly Asp Thr Arg Ala 3490 3495 3500	10512
cgg cgg tcc gac gtg cct gcc cag cgc tcc ggt ggc gtg cct gct cgg Arg Arg Ser Asp Val Pro Ala Gln Arg Ser Gly Gly Val Pro Ala Arg 3505 3510 3515 3520	10560
cgg tcg gtt gat gta tcg ggt cgg gag gtg ttg ccg tgg ttg tcg ggt Arg Ser Val Asp Val Ser Gly Arg Glu Val Leu Pro Trp Leu Ser Gly 3525 3530 3535	10608
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gcg cgg cat ctg gct ggt gtg tgt ggg gtg cgg gat ctg ctg ttg gtg Ala Arg His Leu Ala Gly Val Cys Gly Val Arg Asp Leu Leu Leu Val 3555 3560 3565	10704
agc cgg cgt ggt ccg gat gct ccg ggt gcg gag ggt ctg cgg gcg gag Ser Arg Arg Gly Pro Asp Ala Pro Gly Ala Glu Gly Leu Arg Ala Glu 3570 3575 3580	10752
ctg gcc gcg ttg ggg gcg gag gtg cgg att gtt gcg tgt gat gtg ggg Leu Ala Ala Leu Gly Ala Glu Val Arg Ile Val Ala Cys Asp Val Gly 3585 3590 3595 3600	10800
gag cgg cgg gag gtg gtc cgg ctg ctg gag ggt gtt cct gcc ggg tgt Glu Arg Arg Glu Val Val Arg Leu Leu Glu Gly Val Pro Ala Gly Cys 3605 3610 3615	10848
ccg ctg acg ggt gtc gtg cat gcg gct ggt gtg ctg gac gat gcg acg Pro Leu Thr Gly Val Val His Ala Ala Gly Val Leu Asp Asp Ala Thr 3620 3625 3630	10896
atc gcc tct ctc acg ccc gag cgg ctg ggc acg gtg ttc gcg gcc aag Ile Ala Ser Leu Thr Pro Glu Arg Leu Gly Thr Val Phe Ala Ala Lys 3635 3640 3645	10944
gtg gat gcc gct ctt ttg ctg gat gag ctg acg cgg ggt atg gag ctg Val Asp Ala Ala Leu Leu Leu Asp Glu Leu Thr Arg Gly Met Glu Leu 3650 3655 3660	10992
tcg gcg ttc gtg ctg ttc tcc tcg gcc gcg ggg atc ctg ggg tcg gcc Ser Ala Phe Val Leu Phe Ser Ser Ala Ala Gly Ile Leu Gly Ser Ala 3665 3670 3675 3680	11040
ggg cag ggc aac tac gcc gcg gcc aat gcc gct ctg gac gcg ctg gcg Gly Gln Gly Asn Tyr Ala Ala Ala Asn Ala Ala Leu Asp Ala Leu Ala 3685 3690 3695	11088

tac cgg cgg cgg gcg gcg ggt ctg ccg ggg gtg tcg ctg gcg tgg ggg Tyr Arg Arg Arg Ala Ala Gly Leu Pro Gly Val Ser Leu Ala Trp Gly 3700 3705 3710	11136
ctg tgg gaa gag gcc agc ggg atg acc ggg cac ctg gcc ggc acc gac Leu Trp Glu Glu Ala Ser Gly Met Thr Gly His Leu Ala Gly Thr Asp 3715 3720 3725	11184
cac cgg cgc atc atc cgt tcc ggt ctg cat ccc atg tcg acc ccg gac His Arg Arg Ile Ile Arg Ser Gly Leu His Pro Met Ser Thr Pro Asp 3730 3735 3740	11232
gca ctg gcc ctc ttc gat gcg gcc ctg gct ctg gac cgg ccg gtc ctg Ala Leu Ala Leu Phe Asp Ala Ala Leu Ala Leu Asp Arg Pro Val Leu 3745 3750 3755 3760	11280
ctg ccc gcc gac ctg cgt ccc gcc ccg ccc ctg ccg ccc ctg ctg cag Leu Pro Ala Asp Leu Arg Pro Ala Pro Pro Leu Pro Pro Leu Leu Gln 3765 3770 3775	11328
gac ctc ctg ccc gcc acc cgc cgc cgc acc acc cgc acc acc act acc Asp Leu Leu Pro Ala Thr Arg Arg Arg Thr Thr Arg Thr Thr Thr 3780 3785 3790	11376
ggt ggt gcg gac aac ggc gcc cag ctg cac gcc cgg ctg gcc ggc cag Gly Gly Ala Asp Asn Gly Ala Gln Leu His Ala Arg Leu Ala Gly Gln 3795 3800 3805	11424
aca cac gaa caa cag cac acc acc ctc ctc gcc ctg gtc cgc tcc cac Thr His Glu Gln Gln His Thr Thr Leu Leu Ala Leu Val Arg Ser His 3810 3815 3820	11472
atc gcc acc gtc ctg ggc cac acc acc ccc gac acc atc ccc ccc gac Ile Ala Thr Val Leu Gly His Thr Thr Pro Asp Thr Ile Pro Pro Asp 3825 3830 3835 3840	11520
cgc gcg ttc cgc gac ctc ggc ttc gac tcc ctc acc gcc gtc gaa cta Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu 3845 3850 3855	11568
cgc aac cgg ctc tcc cgc acc acc gga ctc cgc ctc ccc acc acc ctc Arg Asn Arg Leu Ser Arg Thr Thr Gly Leu Arg Leu Pro Thr Thr Leu 3860 3865 3870	11616
gcc ttc gac cac ccc aac ccc acc acc ctc acc cac cac ctc cac aca Ala Phe Asp His Pro Asn Pro Thr Thr Leu Thr His His Leu His Thr 3875 3880 3885	11664
caa ctc cag cca caa ccg gac aac gct gtc gcc ccc gtg ttg gcg gag Gln Leu Gln Pro Gln Pro Asp Asn Ala Val Ala Pro Val Leu Ala Glu 3890 3895 3900	11712
ctc gac aaa ctc gaa tcc gcc ctc tcc gcc ctc gac aaa acc gac agc Leu Asp Lys Leu Glu Ser Ala Leu Ser Ala Leu Asp Lys Thr Asp Ser 3905 3910 3915 3920	11760
gcc agc gaa aga gtc acc ctg cgg ctg aag tca ctc atg ttg agg tgg Ala Ser Glu Arg Val Thr Leu Arg Leu Lys Ser Leu Met Leu Arg Trp 3925 3930 3935	11808

aac gca ccc cag cat ccg aca gcc gaa agc gct gat gac gac gag aag Asn Ala Pro Gln His Pro Thr Ala Glu Ser Ala Asp Asp Asp Glu Lys 3940 3945 3950	11856
ttc aca tcg gca aca gag gct gag att ttc aaa ttc att gac aac gac Phe Thr Ser Ala Thr Glu Ala Glu Ile Phe Lys Phe Ile Asp Asn Asp 3955 3960 3965	11904
ctc ggc ctg tcc tgaaccggac gcctgccact ccgcccgtat ccgctggggc Leu Gly Leu Ser 3970	11956
ctgctaggac gtga atg caa ttg gcg aat gaa gcg aag ctc ctg gaa tac Met Gln Leu Ala Asn Glu Ala Lys Leu Leu Glu Tyr 3975 3980	12006
ctc aag cgc gtc act gcg gac ctg gac cgc act cgc cgt cgc ctg tac Leu Lys Arg Val Thr Ala Asp Leu Asp Arg Thr Arg Arg Arg Leu Tyr 3985 3990 3995 4000	12054
gag gtg gtc gag cgt gag cag gag ccg atc gcg att gtg ggg atg gcg Glu Val Val Glu Arg Glu Gln Glu Pro Ile Ala Ile Val Gly Met Ala 4005 4010 4015	12102
tgt cgt tac cca ggc ggg gcg acg tca ccc acg cga ctg tgg cat ctc Cys Arg Tyr Pro Gly Gly Ala Thr Ser Pro Thr Arg Leu Trp His Leu 4020 4025 4030	12150
gtc aag tcc cag acg gac gct atc ggg gag ttc ccg acc gac cgt gga Val Lys Ser Gln Thr Asp Ala Ile Gly Glu Phe Pro Thr Asp Arg Gly 4035 4040 4045	12198
tgg aac ctg gag cag ctc tac gac ccg gac ccc gac cgc tca gga acc Trp Asn Leu Glu Gln Leu Tyr Asp Pro Asp Pro Asp Arg Ser Gly Thr 4050 4055 4060	12246
agt tac acg cgc agc gga ggg ttt ctc tat gac gcg ggc gac ttc gac Ser Tyr Thr Arg Ser Gly Gly Phe Leu Tyr Asp Ala Gly Asp Phe Asp 4065 4070 4075 4080	12294
gcc gcg ttc ttc gag ttg tca ccg cgt gag gcg ctg gca atg gac ccg Ala Ala Phe Phe Glu Leu Ser Pro Arg Glu Ala Leu Ala Met Asp Pro 4085 4090 4095	12342
cag cag cgc ctg ctg ctc gaa acc act tgg gaa acg ttc gaa cag ggc Gln Gln Arg Leu Leu Leu Glu Thr Thr Trp Glu Thr Phe Glu Gln Gly 4100 4105 4110	12390
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ggg atc aat ccg gag gac tac acc acc gga tac aca cat cag ccc tca Gly Ile Asn Pro Glu Asp Tyr Thr Thr Gly Tyr Thr His Gln Pro Ser 4130 4135 4140	12486
aac gca gtc gag ggc tac ctg ctc act ggc agc gcg gca agc att gcg Asn Ala Val Glu Gly Tyr Leu Leu Thr Gly Ser Ala Ala Ser Ile Ala 4145 4150 4155 4160	12534

ctg acg gag acg gtg ccc tgg ccc ggc ggg gag ggg cgg cta cgg cgg	13302
Leu Thr Glu Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Leu Arg Arg	
4405 4410 4415	
gca gga gtg tca tca ttc ggc gtc agc ggc acc aac gcc cac gtc atc	13350
Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile	
4420 4425 4430	
ctc gag gaa gca ccc gcc cac aac atc ccg tca gac aca ccc gcc gac	13398
Leu Glu Glu Ala Pro Ala His Asn Ile Pro Ser Asp Thr Pro Ala Asp	
4435 4440 4445	
gac gtc ccg gga gaa tca gcc gcc gac gag gat gcc ggt agt ggc gat	13446
Asp Val Pro Gly Glu Ser Ala Ala Asp Glu Asp Ala Gly Ser Gly Asp	
4450 4455 4460	
gag gct gct gcc ggc agt cca ggg gtg tgg ccg tgg ctg gtg tcc gcc	13494
Glu Ala Ala Ala Gly Ser Pro Gly Val Trp Pro Trp Leu Val Ser Ala	
4465 4470 4475 4480	
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Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln Ala Leu His Ala His	
4485 4490 4495	
ctc acc gac cac ccc ggc ctc gac ctc gcc gac gtc ggg tac acc ctc	13590
Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp Val Gly Tyr Thr Leu	
4500 4505 4510	
gcc cac gcc cgc gcc gtg ttc gac cac cgc gcc acc ctc atc gcc gcc	13638
Ala His Ala Arg Ala Val Phe Asp His Arg Ala Thr Leu Ile Ala Ala	
4515 4520 4525	
gac cgc gac acc ttc ctg caa gca ctc cag gca ctc gcc gca ggc gaa	13686
Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala Leu Ala Ala Gly Glu	
4530 4535 4540	
ccc cac ccc gcc gtc atc cac agc agc gcc cca ggc ggg acc ggg acc	13734
Pro His Pro Ala Val Ile His Ser Ser Ala Pro Gly Gly Thr Gly Thr	
4545 4550 4555 4560	
ggg gag gcc gca gga aag acc gca ttc atc tgc tcc gga cag ggc acc	13782
Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys Ser Gly Gln Gly Thr	
4565 4570 4575	
caa cgc ccc ggc atg gcc cac ggc ctc tac cac acc cac ccc gtc ttc	13830
Gln Arg Pro Gly Met Ala His Gly Leu Tyr His Thr His Pro Val Phe	
4580 4585 4590	
gcc gcc gca ctc aac gac atc tgc acc cac ctc gac ccc cac ctc gac	13878
Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu Asp Pro His Leu Asp	
4595 4600 4605	
cac ccc ctc ctc ccc ctc ctc acc cag gac ccc aac acc cag gac acc	13926
His Pro Leu Leu Pro Leu Leu Thr Gln Asp Pro Asn Thr Gln Asp Thr	
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acc acc ctc gaa gaa gcg gcc gca ctg ctc cag cag acc cgc tac gcc	13974
Thr Thr Leu Glu Glu Ala Ala Ala Leu Leu Gln Gln Thr Arg Tyr Ala	
4625 4630 4635 4640	

cag	ccc	gcc	ctc	ttc	gcc	ttc	cag	gtc	gcc	ctc	cac	cgc	ctc	ctc	acc		14022
Gln	Pro	Ala	Leu	Phe	Ala	Phe	Gln	Val	Ala	Leu	His	Arg	Leu	Leu	Thr		
			4645					4650					4655				
gac	ggc	tac	cac	atc	acc	ccc	cac	tac	tac	gcc	gga	cac	tcc	ctc	ggc		14070
Asp	Gly	Tyr	His	Ile	Thr	Pro	His	Tyr	Tyr	Ala	Gly	His	Ser	Leu	Gly		
			4660					4665					4670				
gaa	atc	acc	gcc	gcc	cac	ctc	gcc	ggc	atc	ctc	acc	ctc	acc	gac	gcc		14118
Glu	Ile	Thr	Ala	Ala	His	Leu	Ala	Gly	Ile	Leu	Thr	Leu	Thr	Asp	Ala		
			4675					4680					4685				
acc	acc	ctc	atc	acc	caa	cgc	gcc	acc	ctc	atg	caa	acc	atg	ccc	ccc		14166
Thr	Thr	Leu	Ile	Thr	Gln	Arg	Ala	Thr	Leu	Met	Gln	Thr	Met	Pro	Pro		
			4690				4695				4700						
ggc	acc	atg	acc	acc	ctc	cac	acc	acc	ccc	cac	cac	atc	acc	cac	cac		14214
Gly	Thr	Met	Thr	Thr	Leu	His	Thr	Thr	Pro	His	His	Ile	Thr	His	His		
4705					4710				4715						4720		
ctc	acc	gcc	cac	gaa	aac	gac	ctc	gcc	atc	gcc	gcc	atc	aac	acc	ccc		14262
Leu	Thr	Ala	His	Glu	Asn	Asp	Leu	Ala	Ile	Ala	Ala	Ile	Asn	Thr	Pro		
				4725				4730						4735			
acc	tcc	ctc	gtc	atc	agc	ggc	acc	ccc	cac	acc	gtc	caa	cac	atc	acc		14310
Thr	Ser	Leu	Val	Ile	Ser	Gly	Thr	Pro	His	Thr	Val	Gln	His	Ile	Thr		
			4740					4745					4750				
acc	ctc	tgc	caa	caa	caa	ggc	atc	aaa	acc	aaa	acc	ctc	ccc	acc	aac		14358
Thr	Leu	Cys	Gln	Gln	Gln	Gly	Ile	Lys	Thr	Lys	Thr	Leu	Pro	Thr	Asn		
			4755				4760					4765					
cac	gcc	ttc	cac	tcc	ccc	cac	acc	aac	ccc	atc	ctc	aac	caa	ctc	cac		14406
His	Ala	Phe	His	Ser	Pro	His	Thr	Asn	Pro	Ile	Leu	Asn	Gln	Leu	His		
			4770				4775				4780						
cag	cac	acc	caa	acc	ctc	acc	tac	cac	cca	ccc	cac	acc	ccc	ctc	atc		14454
Gln	His	Thr	Gln	Thr	Leu	Thr	Tyr	His	Pro	Pro	His	Thr	Pro	Leu	Ile		
4785					4790				4795						4800		
acc	gcc	aac	acc	cca	ccc	gac	caa	ctc	ctc	acc	ccc	cac	tac	tgg	acc		14502
Thr	Ala	Asn	Thr	Pro	Pro	Asp	Gln	Leu	Leu	Thr	Pro	His	Tyr	Trp	Thr		
				4805				4810						4815			
caa	caa	gcc	cgc	aac	acc	gtc	gac	tac	gcc	acc	acc	acc	caa	acc	ctc		14550
Gln	Gln	Ala	Arg	Asn	Thr	Val	Asp	Tyr	Ala	Thr	Thr	Thr	Gln	Thr	Leu		
			4820					4825					4830				
cac	caa	cac	ggc	gtc	acc	acc	tac	atc	gaa	ctc	gga	ccc	gac	aac	acc		14598
His	Gln	His	Gly	Val	Thr	Thr	Tyr	Ile	Glu	Leu	Gly	Pro	Asp	Asn			

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ccc ttc caa cac cac cac tac tgg ctc caa cca ccc ggc aag ccg agc Pro Phe Gln His His His Tyr Trp Leu Gln Pro Pro Gly Lys Pro Ser 4915 4920 4925	14838
gac ccg tca ccg agc gaa ggc cgt gag caa gcc acg acc cca tca acc Asp Pro Ser Pro Ser Glu Gly Arg Glu Gln Ala Thr Thr Pro Ser Thr 4930 4935 4940	14886
ccg ctg cgt gat gtc ctc gtg ggc aag tct ccg cag gag cga gac gaa Pro Leu Arg Asp Val Leu Val Gly Lys Ser Pro Gln Glu Arg Asp Glu 4945 4950 4955 4960	14934
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gcc act ccc gaa gtg atc gtt ccg aac aag gcc ttc aaa gag ctg ggt Ala Thr Pro Glu Val Ile Val Pro Asn Lys Ala Phe Lys Glu Leu Gly 4980 4985 4990	15030
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ggc acg acc act cgt ctg ccg cta act gcg gtc ccc gcc gac gag ccg Gly Thr Thr Thr Arg Leu Pro Leu Thr Ala Val Pro Ala Asp Glu Pro 5045 5050 5055	15222
atc gcc atc gtc ggc atg gcc tgt cgg tac ccc ggt gat gta cgg acg Ile Ala Ile Val Gly Met Ala Cys Arg Tyr Pro Gly Asp Val Arg Thr 5060 5065 5070	15270
gtc gat gat ctc tgg cag gtg gtc agt ggt ggc cat gac gcg atc ggc Val Asp Asp Leu Trp Gln Val Val Ser Gly Gly His Asp Ala Ile Gly 5075 5080 5085	15318
gga ttc ccg acg aac cgt ggg tgg gac ctc gac acg ctg tac aac ccg Gly Phe Pro Thr Asn Arg Gly Trp Asp Leu Asp Thr Leu Tyr Asn Pro 5090 5095 5100	15366
gac ccg gac cac cac gga acc agc tac acc cgg agc ggc gga ttc ctt Asp Pro Asp His His Gly Thr Ser Tyr Thr Arg Ser Gly Gly Phe Leu 5105 5110 5115 5120	15414

tac gac gca ggc aat ttc gat ccc gac ttc ttc ggt atc agt ccg cgt	15462
Tyr Asp Ala Gly Asn Phe Asp Pro Asp Phe Phe Gly Ile Ser Pro Arg	
5125 5130 5135	
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Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Thr Ala	
5140 5145 5150	
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Trp Glu Ser Ile Glu His Ala Cys Ile Asn Pro Asp Ser Leu Arg Gly	
5155 5160 5165	
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Thr Pro Thr Gly Val Phe Ala Gly Leu Thr Tyr His Asp Tyr Ala Ala	
5170 5175 5180	
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Arg Phe Pro Thr Ala Pro Ala Gly Phe Glu Gly Tyr Leu Gly His Gly	
5185 5190 5195 5200	
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Ser Ala Gly Ser Ile Ala Ser Gly Arg Val Ala Tyr Ala Leu Gly Leu	
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Glu Gly Pro Ala Leu Thr Val Asp Thr Ala Cys Ser Ser Ser Leu Val	
5220 5225 5230	
gct ctg cac ctg gcc tgt cag gcg ctg cgg tcc ggc gag tgt tcc atg	15798
Ala Leu His Leu Ala Cys Gln Ala Leu Arg Ser Gly Glu Cys Ser Met	
5235 5240 5245	
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Ala Leu Ala Gly Gly Val Thr Val Met Ser Thr Pro Ala Gly Phe Val	
5250 5255 5260	
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Glu Phe Ser Arg Gln Arg Gly Leu Ala Val Asp Gly Arg Cys Lys Ala	
5265 5270 5275 5280	
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Phe Ser Ala Ala Ala Asp Gly Thr Gly Trp Gly Glu Gly Val Gly Met	
5285 5290 5295	
ctg ctg gtg gag cgg ctg tcg gac gcg cgg cgg ctc ggt cac cga atc	15990
Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Leu Gly His Arg Ile	
5300 5305 5310	
ctc gcg gtg gtg cgt ggc agt gcg gtc aat cag gac ggt gcg agc aac	16038
Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn	
5315 5320 5325	
ggg ctg acg gcg ccc aac ggg ccg tcc cag gag cgt gtc atc cgc ctg	16086
Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln Glu Arg Val Ile Arg Leu	
5330 5335 5340	
gcc ctg gcc aac gcg gac ctg acc ccc gcc gac gtc gat gcg gtg gag	16134
Ala Leu Ala Asn Ala Asp Leu Thr Pro Ala Asp Val Asp Ala Val Glu	
5345 5350 5355 5360	

gcc Ala	cac His	ggc Gly	acc Thr	ggc Gly 5365	acc Thr	act Thr	tgt Leu	ggc Gly 5370	gac Asp	ccg Pro	atc Ile	gag Glu	gcc Ala 5375	cag Gln	gcc Ala	16182
ctc Leu	ctc Leu	gcc Ala 5380	acc Thr	tac Tyr	gga Gly	cag Gln	gac Asp	cgc Arg	ccc Pro	ggc Gly	aac Asn	gaa Glu	ccg Pro 5390	ctg Leu	tgg Trp	16230
ctg Leu	ggc Gly 5395	tcg Ser	atg Met	aag Lys	tcg Ser	aac Asn	atc Ile	ggc Gly 5400	cac His	gcg Ala	cag Gln	gct Ala 5405	gcc Ala	gca Ala	ggc Gly	16278
gtg Val 5410	ggc Gly	ggg Gly	gtc Val	atc Ile	aag Lys	atg Met	gtg Val	atg Met	gcg Ala	ctg Leu	cgg Arg	aat Asn	ggc Gly	ctg Leu	ctg Leu	16326
ccg Pro 5425	cgg Arg	acg Thr	ttg Leu	cat His	gtg Val	gat Asp	gag Glu	ccg Pro	tcg Ser	ccg Pro	cat His	gtg Val	gac Asp	tgg Trp	tcc Ser 5440	16374
gcg Ala	ggg Gly	gcg Ala	gtg Val	cag Gln	ctg Leu	ctg Leu	acg Thr	gag Glu 5450	acg Thr	gtg Val	ccc Pro	tgg Trp	ccc Pro	ggc Gly 5455	ggg Gly	16422
gag Glu	ggg Gly	cgg Arg	ctg Leu 5460	cgg Arg	cgg Arg	gca Ala	gga Gly	gtg Val 5465	tca Ser	tcg Ser	ttc Phe	ggc Gly 5470	gtc Val	agc Ser	ggc Gly	16470
acc Thr	aac Asn 5475	gcc Ala	cac His	gtc Val	atc Ile	ctc Leu	gaa Glu	gaa Glu 5480	gca Ala	ccc Pro	gcc Ala	cac His	aac Asn	atc Ile	ccg Pro	16518
tca Ser 5490	gac Asp	aca Thr	ccc Pro	gcc Ala	gac Asp	gac Asp	gcc Ala	ccg Pro	gga Gly	gaa Glu	gca Ala	gcc Ala	gcc Ala	gac Asp	gat Asp	16566
gtt Val 5505	ccg Pro	ggg Gly	gaa Glu	gcg Ala	gcc Ala	ggc Gly	gac Asp	gac Asp	gcc Ala	ggc Gly	acc Thr	ggc Gly	ggg Gly	gaa Glu	gcg Ala 5520	16614
act Thr	ggc Gly	cct Pro	gct Ala	gcc Ala	ggc Gly	agt Ser	cca Pro	ggg Gly 5530	gtg Val	tgg Trp	ccg Pro	tgg Trp	ctg Leu	gtg Val	tcg Ser	16662
gcc Ala	aag Lys	tcg Ser	cag Gln	ccg Pro	gcc Ala	ctg Leu	cgc Arg	gcc Ala 5545	cag Gln	gcc Ala	cag Gln	gcc Ala	ctg Leu 5550	cac His	gcc Ala	16710
cac His	ctc Leu	acc Thr 5555	gac Asp	cac His	ccc Pro	ggc Gly	ctc Leu	gac Asp 5560	ctc Leu	gcc Ala	gac Asp	gtc Val	ggg Gly	tac Tyr	acc Thr	16758
ctc Leu 5570	gcc Ala	cac His	gcc Ala	cgc Arg	gcc Ala	gtg Val	ttc Phe	gac Asp	cac His	cgc Arg	gcc Ala 5580	acc Thr	ctc Leu	atc Ile	gcc Ala	16806
gcc Ala 5585	gac Asp	cgc Arg	gac Asp	acc Thr	ttc Phe	ctg Leu	caa Gln	gca Ala	ctc Leu	cag Gln	gca Ala	ctc Leu	gcc Ala	gca Ala	ggc Gly 5600	16854

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Glu Pro His Pro Ala Val Ile His Ser Ser Ala Pro Gly Gly Thr Gly	
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Thr Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys Ser Gly Gln Gly	
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acc caa cgc ccc ggc atg gcc cac ggc ctc tac cac acc cac ccc gtc	16998
Thr Gln Arg Pro Gly Met Ala His Gly Leu Tyr His Thr His Pro Val	
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ttc gcc gcc gca ctc aac gac atc tgc acc cac ctc gac ccc cac ctc	17046
Phe Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu Asp Pro His Leu	
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Asp His Pro Leu Leu Pro Leu Leu Thr Gln Asp Pro Asn Thr Gln Asp	
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Thr Thr Thr Leu Glu Ala Ala Ala Leu Leu Gln Gln Thr Pro Tyr	
5685 5690 5695	
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Ala Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu	
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Thr Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu	
5715 5720 5725	
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Gly Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp	
5730 5735 5740	
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Ala Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro	
5745 5750 5755 5760	
ccc ggc acc atg acc acc ctc cac acc acc ccc cac cac atc acc cac	17382
Pro Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His	
5765 5770 5775	
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His Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr	
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Pro Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile	
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Thr Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr	
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aaa aac gcc ttc cac tcc ccc cac acc aac ccc atc ctc aac caa ctc	17574
Lys Asn Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu	
5825 5830 5835 5840	

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atc acc gcc aac acc cca ccc gac caa ctc ctc acc ccc cac tac tgg Ile Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp 5860 5865 5870	17670
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ctc cac caa cac ggc gtc acc acc tac atc gaa ctc gga ccc gac aac Leu His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn 5890 5895 5900	17766
acc ctc acc acc ctc acc cac cac aac ctc ccc aac acc ccc acc acc Thr Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Thr Pro Thr Thr 5905 5910 5915 5920	17814
acc ctc acc ctc acc cac ccc cac cac cac ccc caa acc cac ctc ctc Thr Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu 5925 5930 5935	17862
acc aac ctc gcc aaa acc acc acc acc tgg cac ccc cac cac tac acc Thr Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr 5940 5945 5950	17910
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tac ccc ttc caa cac cag cac tac tgg ctc gaa agc aca cag ccg ggt Tyr Pro Phe Gln His Gln His Tyr Trp Leu Glu Ser Thr Gln Pro Gly 5970 5975 5980	18006
gcc gga tcc ggt tcg ggt tcc ggt tcc ggg cgg gca ggg act gcg ggc Ala Gly Ser Gly Ser Gly Ser Gly Ser Gly Arg Ala Gly Thr Ala Gly 5985 5990 5995 6000	18054
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gac ctg gaa acg gtc gcg acc acg ctc gcc gtg ccc ccc tcc gcc ggc Asp Leu Glu Thr Val Ala Thr Thr Leu Ala Val Pro Pro Ser Ala Gly 6020 6025 6030	18150
ctg gac acg gtg gtg ccc gca ctc tcc gcc tgg cac cgc cac caa cac Leu Asp Thr Val Val Pro Ala Leu Ser Ala Trp His Arg His Gln His 6035 6040 6045	18198
gac caa gcc cgc atc aac acc tgg acc tac cag gaa acc tgg aaa ccc Asp Gln Ala Arg Ile Asn Thr Trp Thr Tyr Gln Glu Thr Trp Lys Pro 6050 6055 6060	18246
ctc acc ctc ccc acc acc cac caa ccc cac caa acc tgg ctc atc gcc Leu Thr Leu Pro Thr Thr His Gln Pro His Gln Thr Trp Leu Ile Ala 6065 6070 6075 6080	18294

atc ccc gaa acc cag acc cac cac ccc cac atc acc aac atc ctc acc Ile Pro Glu Thr Gln Thr His His Pro His Ile Thr Asn Ile Leu Thr 6085 6090 6095	18342
aac ctc cac cac cac ggc atc acc ccc atc ccc ctc acc ctc aac cac Asn Leu His His His Gly Ile Thr Pro Ile Pro Leu Thr Leu Asn His 6100 6105 6110	18390
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gac gaa aca ccc cac ccc cac cac ccc cac aca ccc acc ggc acc ctc Asp Glu Thr Pro His Pro His His Pro His Thr Pro Thr Gly Thr Leu 6145 6150 6155 6160	18534
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Glu Ala Ile Pro Pro Gly Arg Leu Phe Arg Asp Leu Gly Phe Asp Ser	
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Leu Ala Ala Val Glu Leu Arg Asn His Leu Ala Ala Gln Thr Glu Leu	
6595 6600 6605	
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Gly His Phe Asp Ala Glu Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu	
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Ile Glu His Ala Gly Ile Asn Pro His Thr Leu His Gly Thr Pro Thr	
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Gly Val Phe Thr Gly Thr Asn Gly Gln Asp His Ala Ala His Ile Arg	
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Pro Arg Arg Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala	
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His Val Ile Leu Glu Glu Ala Pro Ala Asp Asp Val Pro Gly Gly Pro	
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Pro Ala Asp Glu Asp Ala Gly Ser Gly Glu Glu Ala Ala Ala Gly Ser	
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Pro Gly Val Trp Pro Trp Leu Val Ser Ala Lys Ser Gln Pro Ala Leu	
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Arg Ala Gln Ala Gln Ala Leu His Ala His Leu Thr Asp His Pro Gly	
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Leu Asp Leu Ala Asp Val Gly Tyr Thr Leu Ala His Ala Arg Ala Val	
7140 7145 7150	
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Phe Asp His Arg Ala Thr Leu Ile Ala Ala Asp Arg Asp Thr Phe Leu	
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Gln Ala Leu Gln Ala Leu Ala Ala Gly Glu Pro His Pro Ala Val Ile	
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His Ser Ser Ala Pro Gly Gly Thr Gly Thr Gly Glu Ala Ala Gly Lys	
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Thr Ala Phe Ile Cys Ser Gly Gln Gly Thr Gln Arg Pro Gly Met Ala	
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His Gly Leu Tyr His Thr His Pro Val Phe Ala Ala Ala Leu Asn Asp	
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Ile Cys Thr His Leu Asp Pro His Leu Asp His Pro Leu Leu Pro Leu	
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His Pro His His Tyr Thr His His His Asn Gln Pro His Thr His Thr	
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His Leu Asp Leu Pro Thr Tyr Pro Phe Gln His His His Tyr Trp Leu	
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Ala	Ala	Asn	Ala	Tyr	Leu	Asp	Ala	Leu	Ala	Thr	His	Arg	Gln	Thr	His	
			8005						8010			8015				
gga	ctt	ccc	ggg	gca	tcg	atc	gcc	tgg	ggc	ccc	tgg	gcc	gga	aag	ggc	24150
Gly	Leu	Pro	Gly	Ala	Ser	Ile	Ala	Trp	Gly	Pro	Trp	Ala	Gly	Lys	Gly	
			8020						8025			8030				
atg	tcg	gcc	ggt	gat	gcg	gct	cat	ggt	tac	ctg	gaa	aag	cgc	ggc	att	24198
Met	Ser	Ala	Gly	Asp	Ala	Ala	His	Gly	Tyr	Leu	Glu	Lys	Arg	Gly	Ile	
			8035						8040			8045				
ctg	ccg	atg	gag	cca	cgc	atg	gcg	ctc	gcg	gca	ttc	cat	cgt	gcg	cgg	24246
Leu	Pro	Met	Glu	Pro	Arg	Met	Ala	Leu	Ala	Ala	Phe	His	Arg	Ala	Arg	
			8050						8055			8060				
gcg	cag	cgg	ccg	aat	tcc	aac	ctg	atc	atc	gcg	gac	atc	gac	tgg	gag	24294
Ala	Gln	Arg	Pro	Asn	Ser	Asn	Leu	Ile	Ile	Ala	Asp	Ile	Asp	Trp	Glu	
8065			8070						8075			8080				
cgc	ttc	gtc	ccc	gcc	ttc	acc	gct	cga	cgc	cac	agc	ccg	ctc	atc	gag	24342
Arg	Phe	Val	Pro	Ala	Phe	Thr	Ala	Arg	Arg	His	Ser	Pro	Leu	Ile	Glu	
			8085						8090			8095				
gac	att	ccg	gag	gtt	cgg	caa	gcg	gct	cag	gag	ctg	gaa	gca	gct	gcg	24390
Asp	Ile	Pro	Glu	Val	Arg	Gln	Ala	Ala	Gln	Glu	Leu	Glu	Ala	Ala	Ala	
			8100						8105			8110				
tcg	acg	gca	aag	acg	acc	aca	gct	cag	ccg	att	gcg	acg	tct	ctc	cgt	24438
Ser	Thr	Ala	Lys	Thr	Thr	Thr	Ala	Gln	Pro	Ile	Ala	Thr	Ser	Leu	Arg	
8115						8120						8125				
gag	cga	ttg	gcc	cga	ctg	acg	tcc	tca	aag	cag	aac	cag	gtg	ctg	ctc	24486
Glu	Arg	Leu	Ala	Arg	Leu	Thr	Ser	Ser	Lys	Gln	Asn	Gln	Val	Leu	Leu	
8130						8135						8140				
ggc	ctg	att	cgg	aca	ggc	atc	tgc	acc	gtt	ctc	ggc	ctt	cgt	aat	ccg	24534
Gly	Leu	Ile	Arg	Thr	Gly	Ile	Cys	Thr	Val	Leu	Gly	Leu	Arg	Asn	Pro	
8145			8150						8155			8160				
gaa	ggc	atc	gag	gac	caa	cga	gcc	ttc	cgc	gac	ctc	ggc	ttc	gac	tcg	24582
Glu	Gly	Ile	Glu	Asp	Gln	Arg	Ala	Phe	Arg	Asp	Leu	Gly	Phe	Asp	Ser	
			8165						8170			8175				
ctg	acg	tcg	gct	cag	ttc	agc	aag	gaa	ctc	gcc	aag	gaa	acc	gga	ctg	24630
Leu	Thr	Ser	Ala	Gln	Phe	Ser	Lys	Glu	Leu	Ala	Lys	Glu	Thr	Gly	Leu	
			8180						8185			8190				
cca	ctc	ccc	ccg	tcc	ctg	gtc	ttc	gac	tat	ccc	acc	ccg	cag	gaa	tgt	24678
Pro	Leu	Pro	Pro	Ser	Leu	Val	Phe	Asp	Tyr	Pro	Thr	Pro	Gln	Glu	Cys	
8195						8200						8205				
gct	gcc	cat	ctg	cgc	aca	caa	ctc	gtc	gac	cta	gac	gac	gaa	gag	gac	24726
Ala	Ala	His	Leu	Arg	Thr	Gln	Leu	Val	Asp	Leu	Asp	Asp	Glu	Glu	Asp	
8210						8215						8220				
gcg	gca	ctg	tcg	aat	gct	ctc	ccg	caa	gtg	gcc	cat	cgg	cgt	acc	gtc	24774
Al																

gag Glu	gac Asp	gaa Glu	ccg Pro	atc Ile 8245	gcc Ala	atc Ile	atc Ile	ggg Gly	atg Met 8250	gca Ala	tgt Cys	cgc Arg	ttc Phe 8255	ccc Pro	ggc Gly	24822
ggc Gly	gta Val	cgt Arg	tct Ser 8260	gcc Ala	gac Asp	gac Asp	ctg Leu	tgg Trp 8265	gaa Glu	ttg Leu	ctc Leu	gct Ala	tcg Ser 8270	ggg Gly	aag Lys	24870
gac Asp	gct Ala	atc Ile 8275	ggc Gly	gtc Val	ttc Phe	ccg Pro	acc Thr 8280	gac Asp	cgc Arg	ggc Gly	tgg Trp	gac Asp 8285	ctg Leu	gac Asp	acg Thr	24918
ctc Leu 8290	tac Tyr	gac Asp	ccc Pro	gac Asp	ccc Pro 8295	gac Asp	cac His	ccc Pro	ggc Gly	acc Thr 8300	tgc Cys	tac Tyr	acc Thr	cga Arg	aac Asn	24966
ggc Gly 8305	gga Gly	ttc Phe	ctc Leu	tac Tyr 8310	ggc Gly	gca Ala	ggc Gly	cac His	ttc Phe 8315	gac Asp	gcc Ala	gaa Glu	ttc Phe	ttc Phe	ggc Gly 8320	25014
atc Ile	agc Ser	ccc Pro	cgc Arg 8325	gaa Glu	gcc Ala	ctc Leu	gcc Ala	atg Met 8330	gac Asp	ccc Pro	cag Gln	caa Gln	cga Arg 8335	ctc Leu	ctc Leu	25062
ctc Leu	gaa Glu	acc Thr 8340	gcc Ala	tgg Trp	gaa Glu	acc Thr	atc Ile 8345	gaa Glu	cac His	gcc Ala	ggc Gly	atc Ile 8350	aac Asn	ccc Pro	cac His	25110
acc Thr	ctc Leu 8355	cac His	ggc Gly	acc Thr	ccc Pro	acc Thr 8360	gga Gly	gtc Val	ttc Phe	gcc Ala	gga Gly	atc Ile 8365	aac Asn	gct Ala	caa Gln	25158
gac Asp 8370	cac His	gcc Ala	gcg Ala	cat His	atc Ile 8375	cgc Arg	caa Gln	agc Ser	cgt Arg	gat Asp 8380	gtg Val	gag Glu	acc Thr	atc Ile	gag Glu	25206
ggc Gly 8385	tac Tyr	gcc Ala	ctg Leu	acc Thr 8390	ggc Gly	agt Ser	tcg Ser	gga Gly	agt Ser 8395	gtg Val	gcg Ala	tcc Ser	ggc Gly	cgg Arg	gtg Val 8400	25254
gcc Ala	tac Tyr	acg Thr	ctc Leu 8405	ggg Gly	ctc Leu	gaa Glu	ggc Gly	ccc Pro 8410	gcg Ala	gtg Val	tcg Ser	gtg Val	gat Asp 8415	acg Thr	gcg Ala	25302
tgt Cys	tcg Ser	tcg Ser	tcg Ser 8420	ttg Leu	gtg Val	gcg Ala	ttg Leu	cat His 8425	tgg Trp	gcg Ala	gcg Ala	cag Gln 8430	gcg Ala	ttg Leu	cgt Arg	25350
gcg Ala	ggg Gly 8435	gag Glu	tgt Cys	tcg Ser	atg Met	gcg Ala	ctt Leu 8440	gcc Ala	ggg Gly	ggg Gly	gtg Val	acg Thr 8445	gtg Val	atg Met	tcg Ser	25398
tct Ser 8450	ccg Pro	ggg Gly	acg Thr	ttt Phe	gtg Val	gag Glu 8455	ttc Phe	tca Ser	cgt Arg	cag Gln 8460	cgg Arg	ggg Gly	ctg Leu	gcc Ala	gcg Ala	25446
gac Asp 8465	ggg Gly	cgg Arg	tgc Cys	aag Lys 8470	gcc Ala	tat Tyr	tcg Ser	gcg Ala	gct Ala 8475	gct Ala	gac Asp	ggg Gly	acc Thr	ggc Gly	tgg Trp 8480	25494

gcc gag ggt gtg ggg atg ctg ctg gtg gag cgg ctc tcc gac gcc cgt	25542
Ala Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Arg	
8485 8490 8495	
cgc aac ggt cac cgt gtc ctg gcc gtg gtg cgt ggc agt gcg gtc aac	25590
Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn	
8500 8505 8510	
cag gac ggt gcg agc aac ggt ctg acc gcg ccc aac ggg ccc tcc cag	25638
Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln	
8515 8520 8525	
cag cgt gtc atc cgt cag gcc ctg gcc aat gcg gga ctg acc ccg gcc	25686
Gln Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Thr Pro Ala	
8530 8535 8540	
gat gtc gac gca gtg gag ggc cac ggc acc ggg acc act ctg ggg gac	25734
Asp Val Asp Ala Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly Asp	
8545 8550 8555 8560	
ccg atc gag gcc cag gca ctc ctg gcc gcc tac gga caa cac cgc ccc	25782
Pro Ile Glu Ala Gln Ala Leu Leu Ala Ala Tyr Gly Gln His Arg Pro	
8565 8570 8575	
cac cac cgc ccc ttg tgg ctg gga tcc ctc aaa tcc aac atc ggg cac	25830
His His Arg Pro Leu Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His	
8580 8585 8590	
gca cag gcc gcc gcg ggc gtg ggc gga gtc atc aag atg gtg atg gcc	25878
Ala Gln Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala	
8595 8600 8605	
ctg cgc aac ggg ctg ctg cca cag acc ctc cac gtg gac gag ccc acc	25926
Leu Arg Asn Gly Leu Leu Pro Gln Thr Leu His Val Asp Glu Pro Thr	
8610 8615 8620	
ccc cag gtc gac tgg tcc aca ggc gca gta caa ctc ctg aca caa ccg	25974
Pro Gln Val Asp Trp Ser Thr Gly Ala Val Gln Leu Leu Thr Gln Pro	
8625 8630 8635 8640	
gtg ccc tgg ccc gcc gac ccg gcc ggc cgg cca cgc cac gcc ggc gtg	26022
Val Pro Trp Pro Ala Asp Pro Ala Gly Arg Pro Arg His Ala Gly Val	
8645 8650 8655	
tca tca ttc ggc gtc agc ggc acc aac gcc cac atc atc ctc gaa gaa	26070
Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Ile Ile Leu Glu Glu	
8660 8665 8670	
gca ccc act ccc cag gac agc gat acc gac gac gaa ccg cct gcc aac	26118
Ala Pro Thr Pro Gln Asp Ser Asp Thr Asp Asp Glu Pro Pro Ala Asn	
8675 8680 8685	
gca cca gcc ctg ccc cat ccc ctc cct ctt ccc gtg ccg gtg tcg gcg	26166
Ala Pro Ala Leu Pro His Pro Leu Pro Leu Pro Val Pro Val Ser Ala	
8690 8695 8700	
agg tct gag gcc ggg ttg cgg gcg cag gca cag gcg ttg cgc cag tac	26214
Arg Ser Glu Ala Gly Leu Arg Ala Gln Ala Gln Ala Leu Arg Gln Tyr	
8705 8710 8715 8720	

gtg	gca	gcc	cgc	ccg	gac	atg	tca	cct	gcc	gac	att	ggt	gcg	ggt	ctg	26262
Val	Ala	Ala	Arg	Pro	Asp	Met	Ser	Pro	Ala	Asp	Ile	Gly	Ala	Gly	Leu	
			8725						8730					8735		
gcc	cgc	ggc	cgg	gcc	gta	ctg	gaa	cac	cgc	gcc	gtc	atc	ctg	gcc	gcg	26310
Ala	Arg	Gly	Arg	Ala	Val	Leu	Glu	His	Arg	Ala	Val	Ile	Leu	Ala	Ala	
			8740					8745					8750			
gac	cgc	gag	gaa	ctg	gcg	cag	gca	ctg	aca	gcc	ctg	gca	gcc	ggc	gaa	26358
Asp	Arg	Glu	Glu	Leu	Ala	Gln	Ala	Leu	Thr	Ala	Leu	Ala	Ala	Gly	Glu	
		8755					8760					8765				
ccc	cac	ccc	cac	atc	acc	aca	ggc	cac	acc	cgg	ggc	ggt	gac	cgc	ggc	26406
Pro	His	Pro	His	Ile	Thr	Thr	Gly	His	Thr	Arg	Gly	Gly	Asp	Arg	Gly	
	8770					8775				8780						
ggc	gtc	gtc	ttc	gtc	ttc	ccc	gga	cag	ggc	ggc	cag	tgg	gcc	ggg	atg	26454
Gly	Val	Val	Phe	Val	Phe	Pro	Gly	Gln	Gly	Gly	Gln	Trp	Ala	Gly	Met	
8785					8790				8795						8800	
ggc	ctg	acc	ctg	ctc	acc	tcc	tca	ccc	gtg	ttc	gcc	gaa	cac	atc	gac	26502
Gly	Leu	Thr	Leu	Leu	Thr	Ser	Ser	Pro	Val	Phe	Ala	Glu	His	Ile	Asp	
			8805					8810						8815		
gca	tgc	gag	aaa	gcc	ctc	acc	ccc	tgg	gtg	ccc	tgg	tcc	ctg	acc	gac	26550
Ala	Cys	Glu	Lys	Ala	Leu	Thr	Pro	Trp	Val	Pro	Trp	Ser	Leu	Thr	Asp	
		8820					8825					8830				
atc	ctg	cac	cgc	gac	ccc	gac	gac	ccc	gca	tgg	caa	caa	gcc	gac	gtg	26598
Ile	Leu	His	Arg	Asp	Pro	Asp	Asp	Pro	Ala	Trp	Gln	Gln	Ala	Asp	Val	
	8835					8840					8845					
gtc	cag	ccc	gtg	ctc	ttc	agc	atc	atg	gtc	tcc	ctc	gcc	gcc	ctg	tgg	26646
Val	Gln	Pro	Val	Leu	Phe	Ser	Ile	Met	Val	Ser	Leu	Ala	Ala	Leu	Trp	
8850					8855					8860						
cgc	tcc	tac	ggc	atc	gaa	ccc	gac	gcg	gtc	ctc	ggc	cac	tcc	cag	gga	26694
Arg	Ser	Tyr	Gly	Ile	Glu	Pro	Asp	Ala	Val	Leu	Gly	His	Ser	Gln	Gly	
8865				8870				8875						8880		
gaa	atc	gcc	gcc	gcc	cac	atc	tgc	ggc	gca	ctc	agc	ctg	aaa	gac	gcc	26742
Glu	Ile	Ala	Ala	Ala	His	Ile	Cys	Gly	Ala	Leu	Ser	Leu	Lys	Asp	Ala	
		8885						8890					8895			
gcc	aaa	acc	gtt	gca	ctg	cgc	agc	cgc	gca	ctg	gcc	gcc	gta	cga	ggc	26790
Ala	Lys	Thr	Val	Ala	Leu	Arg	Ser	Arg	Ala	Leu	Ala	Ala	Val	Arg	Gly	
		8900				8905						8910				
cgg	ggc	gcc	atg	gcc	tca	ctg	ccc	ctg	ccc	gcc	cag	gac	gtg	cag	cag	26838
Arg	Gly	Ala	Met	Ala	Ser	Leu	Pro	Leu	Pro	Ala	Gln	Asp	Val	Gln	Gln	

gtg ctg gcg cac tgc acc gac acc ggc cta cgg gcc aaa cgc atc ccc Val Leu Ala His Cys Thr Asp Thr Gly Leu Arg Ala Lys Arg Ile Pro 8965 8970 8975	26982
gtc gac tac gcc tcc cac tgc ccc cac gtc caa ccc ctc cac gac gaa Val Asp Tyr Ala Ser His Cys Pro His Val Gln Pro Leu His Asp Glu 8980 8985 8990	27030
ctc ctg cac ctg ctg gga gac atc acc ccc cag ccg tcc acc gtg ccg Leu Leu His Leu Leu Gly Asp Ile Thr Pro Gln Pro Ser Thr Val Pro 8995 9000 9005	27078
ttc ttc tcc acc gtg gaa ggc acc tgg ctg gac acc aca acc ctg gac Phe Phe Ser Thr Val Glu Gly Thr Trp Leu Asp Thr Thr Thr Leu Asp 9010 9015 9020	27126
gcc gcc tac tgg tac cgc aac ctc cac cag ccc gtc cgc ttc agc cac Ala Ala Tyr Trp Tyr Arg Asn Leu His Gln Pro Val Arg Phe Ser His 9025 9030 9035 9040	27174
gcc atc cag acc ctg acc gac gac gga cac cgc gcc ttc atc gaa atc Ala Ile Gln Thr Leu Thr Asp Asp Gly His Arg Ala Phe Ile Glu Ile 9045 9050 9055	27222
agc ccc cac ccc acc ctc gtc ccc gcc atc gaa gac acc acc gaa aac Ser Pro His Pro Thr Leu Val Pro Ala Ile Glu Asp Thr Thr Glu Asn 9060 9065 9070	27270
acc acc gaa aac atc acc gcg acc ggc agc ctc cgc cgc ggc gac aac Thr Thr Glu Asn Ile Thr Ala Thr Gly Ser Leu Arg Arg Gly Asp Asn 9075 9080 9085	27318
gac acc cac cgc ttc ctc acc gcc ctc gcc cac acc cac acc acc ggc Asp Thr His Arg Phe Leu Thr Ala Leu Ala His Thr His Thr Thr Gly 9090 9095 9100	27366
atc ggc aca ccc acc acc tgg cac cac cac tac acc caa acc cac ccc Ile Gly Thr Pro Thr Thr Trp His His His Tyr Thr Gln Thr His Pro 9105 9110 9115 9120	27414
cac ccc aac ccc cac acc cac ctc gac ctg ccc acc tac ccc ttc caa His Pro Asn Pro His Thr His Leu Asp Leu Pro Thr Tyr Pro Phe Gln 9125 9130 9135	27462
cac cag cac tac tgg ctc caa cca ccc acc aca aca acc gac ctc acc His Gln His Tyr Trp Leu Gln Pro Pro Thr Thr Thr Thr Asp Leu Thr 9140 9145 9150	27510
acc acc ggc ctc acc ccc acc cac cac ccc ctc ctc acc gcc aca ctc Thr Thr Gly Leu Thr Pro Thr His His Pro Leu Leu Thr Ala Thr Leu 9155 9160 9165	27558
acc ctc gcc gac aac aac aca caa cta ctc acc ggc cgc ctc tcc cta Thr Leu Ala Asp Asn Asn Thr Gln Leu Leu Thr Gly Arg Leu Ser Leu 9170 9175 9180	27606
cgc acc cac ccc tgg ctc acc gac cac acc gtc gcc ggc atg gtc ctc Arg Thr His Pro Trp Leu Thr Asp His Thr Val Ala Gly Met Val Leu 9185 9190 9195 9200	27654

ctg ccg ggc acc gcg ctc ctc gaa ctc gcc ctc caa gcc ggc gaa cgg	27702
Leu Pro Gly Thr Ala Leu Leu Glu Leu Ala Leu Gln Ala Gly Glu Arg	
9205 9210 9215	
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Val Asp Cys Pro Arg Val Glu Glu Leu Thr Leu His Ala Pro Leu Val	
9220 9225 9230	
atc ccg cac acc gag gac gtg acg ttg cag gtc acc gtt cgg gca gcc	27798
Ile Pro His Thr Glu Asp Val Thr Leu Gln Val Thr Val Arg Ala Ala	
9235 9240 9245	
gat gag agt ggc cat cgc gcc ctc gcg atc cac tcg tac tcc ggc acc	27846
Asp Glu Ser Gly His Arg Ala Leu Ala Ile His Ser Tyr Ser Gly Thr	
9250 9255 9260	
gcg tcg tcg gcg gac cgg gag tgg acc cgt cac gcc acg ggc ctc ctc	27894
Ala Ser Ser Ala Asp Arg Glu Trp Thr Arg His Ala Thr Gly Leu Leu	
9265 9270 9275 9280	
aca cac cac gcc gac acc gat cac cgt gcc gac acg cac acg gac gcg	27942
Thr His His Ala Asp Thr Asp His Arg Ala Asp Thr His Thr Asp Ala	
9285 9290 9295	
tgc ctt ggc ggg agc tgg ccc ccg ccc ggc gcg cag ccc atc gaa ctg	27990
Cys Leu Gly Gly Ser Trp Pro Pro Pro Gly Ala Gln Pro Ile Glu Leu	
9300 9305 9310	
ggc gac gtc tac ggt cgt atg gcg gcg gac tcg gac atc gcc tac ggg	28038
Gly Asp Val Tyr Gly Arg Met Ala Ala Asp Ser Asp Ile Ala Tyr Gly	
9315 9320 9325	
ccg gtc ttc cag ggg ctg cac gcc gcc tgg agg ttc ggc gac gat gtc	28086
Pro Val Phe Gln Gly Leu His Ala Ala Trp Arg Phe Gly Asp Asp Val	
9330 9335 9340	
ctg gcc gag gtg cgt ctg ccg gaa gag gct ctg cgc gat gct ccg gcg	28134
Leu Ala Glu Val Arg Leu Pro Glu Glu Ala Leu Arg Asp Ala Pro Ala	
9345 9350 9355 9360	
gcg gcc ttc ggt gtt cac ccg gcc ttg ctc gac gcg gcc ctg cac gcc	28182
Ala Ala Phe Gly Val His Pro Ala Leu Leu Asp Ala Ala Leu His Ala	
9365 9370 9375	
acg gcg ctc acc ccc cag aac ggg gac ggc tcg acg gag aac gtc gcc	28230
Thr Ala Leu Thr Pro Gln Asn Gly Asp Gly Ser Thr Glu Asn Val Ala	
9380 9385 9390	
cag gag agc atg cct gac cgc gca gcc cac cag gcg cga ctg ccg ttc	28278
Gln Glu Ser Met Pro Asp Arg Ala Ala His Gln Ala Arg Leu Pro Phe	
9395 9400 9405	
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Ser Trp Ser Gly Val Ser Leu His Thr Ala Gly Ser Ser Val Leu Arg	
9410 9415 9420	
gta cgg ctg tcg cgc agt ccg cag cac ggt aat gcc gtg gcc ctc acc	28374
Val Arg Leu Ser Arg Ser Pro Gln His Gly Asn Ala Val Ala Leu Thr	
9425 9430 9435 9440	

gcg gcc gac gag gac ggt cgg ccg gtg gtg acg atc gag tcg ctc gcg	28422
Ala Ala Asp Glu Asp Gly Arg Pro Val Val Thr Ile Glu Ser Leu Ala	
9445 9450 9455	
ctg cgg ccg gtg tcc acc gag gag ctg cgc gcg gcc gcg gat cgt acg	28470
Leu Arg Pro Val Ser Thr Glu Glu Leu Arg Ala Ala Ala Asp Arg Thr	
9460 9465 9470	
ccc gag cac gag tcg ctc ttc cga ctg gac tgg gtt tcc gta cca gtg	28518
Pro Glu His Glu Ser Leu Phe Arg Leu Asp Trp Val Ser Val Pro Val	
9475 9480 9485	
ccc gcc aac gcc cct tcg ccc acc gcg gac cgg ccc tgg gcg gtc atc	28566
Pro Ala Asn Ala Pro Ser Pro Thr Ala Asp Arg Pro Trp Ala Val Ile	
9490 9495 9500	
ggc gcg ggc ctt ccc cac ctg ccc ggc ctg acg gag cac gag cac gtg	28614
Gly Ala Gly Leu Pro His Leu Pro Gly Leu Thr Glu His Glu His Val	
9505 9510 9515 9520	
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Thr Ala Tyr Asp Glu Pro Ala Asp Leu Leu Ala Leu Asp Arg Gly	
9525 9530 9535	
gct ccg ccg ccc ggt gtg ctg gtc gta ggt ggt gtc gcc cac acc gaa	28710
Ala Pro Pro Pro Gly Val Leu Val Val Gly Gly Val Ala His Thr Glu	
9540 9545 9550	
gcc ccg gag tat tcc gcc gaa gcc ccc ggg gag cgc ggg acc gag gcc	28758
Ala Arg Glu Tyr Ser Ala Glu Ala Pro Gly Glu Arg Gly Thr Glu Ala	
9555 9560 9565	
tgc gag gcc ccg ccg gac gtc gtg cac gtg ggc gtc gtg cac acg gct	28806
Cys Glu Ala Arg Pro Asp Val Val His Val Gly Val Val His Thr Ala	
9570 9575 9580	
gcc gtg cac gcg gct gcc gcg cag atg ttg gcc agg ctc cag gcc tgg	28854
Ala Val His Ala Ala Ala Ala Gln Met Leu Ala Arg Leu Gln Ala Trp	
9585 9590 9595 9600	
ctg ggc gac gag cgc ctc gca gac agc ccg ctg ctc gtc ctg acg tgc	28902
Leu Gly Asp Glu Arg Leu Ala Asp Ser Arg Leu Leu Val Leu Thr Cys	
9605 9610 9615	
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Gly Ala Val Ala Arg Ala Ser Gly Asp Asp Ala Thr Asp Leu Pro Gly	
9620 9625 9630	
gcc gcc gtg tgg ggg ctg gtg cgt tcg gcg cag tcc gag cac ccg gac	28998
Ala Ala Val Trp Gly Leu Val Arg Ser Ala Gln Ser Glu His Pro Asp	
9635 9640 9645	
cgc atc acg ctg ctg gac ttc gag ccg ggc aca gag gcg gag ccc ggt	29046
Arg Ile Thr Leu Leu Asp Phe Glu Arg Gly Thr Glu Ala Glu Pro Gly	
9650 9655 9660	
cag ctg gcg acg gcg ctg aac tgc ggg gag ccg cag ctt gcc gtc cgc	29094
Gln Leu Ala Thr Ala Leu Asn Cys Gly Glu Arg Gln Leu Ala Val Arg	
9665 9670 9675 9680	

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acc Thr 7055	ggc Gly 7055	acc Thr 7055	act Thr 7055	ttg Leu 7060	ggc Gly 7060	gac Asp 7060	ccg Pro 7060	atc Ile 7060	gag Glu 7065	gcc Ala 7065	cag Gln 7065	gcc Ala 7070	ctc Leu 7070	ctt Leu 7070	gcg Ala 7070	21390
acc Thr 7075	tac Tyr 7075	ggg Gly 7075	cag Gln 7075	gac Asp 7075	cgt Arg 7075	gcc Ala 7080	ggc Gly 7080	gag Glu 7080	ggg Gly 7080	ccg Pro 7085	ctg Leu 7085	tgg Trp 7085	ctg Leu 7085	ggc Gly 7085	tcg Ser 7085	21438
gtc Val 7090	aag Lys 7090	tcc Ser 7090	aat Asn 7090	gtc Val 7095	ggg Gly 7095	cac His 7095	aca Thr 7095	cag Gln 7095	gct Ala 7100	gcc Ala 7100	gcg Ala 7100	ggc Gly 7100	gtc Val 7100	gcc Ala 7100	ggg Gly 7100	21486
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Ile	Arg	Gln	Ala	Leu	Ala	Cys	Ala	Gly	Leu	Ser	Val	Ala	Asp	Val	Asp	
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Val Gly Asp Gly Cys Gly Val Glu Leu Pro Thr Tyr Ala Phe Glu Arg	
915 920 925	
gag cga ttt tgg ctg gac gtg gag gag gga tct gcg gga ggt tcc ggg	2832
Glu Arg Phe Trp Leu Asp Val Glu Glu Gly Ser Ala Gly Gly Ser Gly	
930 935 940	
gtt tcc ggg atg tgg ggt ggt ccg ttg tgg gag gcg gtc gag tgt ggt	2880
Val Ser Gly Met Trp Gly Gly Pro Leu Trp Glu Ala Val Glu Cys Gly	
945 950 955 960	
gat gcg ggg gtg gtg gca tgc ctc ctt ggg gtg gat gag ggg gcg tcg	2928
Asp Ala Gly Val Val Ala Ser Leu Leu Gly Val Asp Glu Gly Ala Ser	
965 970 975	
ctg ggt gcg gtg gtg tgc gcg ttg ggg gaa tgg ggg ccg gta ccg cac	2976
Leu Gly Ala Val Val Ser Ala Leu Gly Glu Trp Gly Arg Val Arg His	
980 985 990	
gag cgt gaa gtg gtg gac ggg tgg cgc tat ccg gag gtg tgg cga ccc	3024
Glu Arg Glu Val Val Asp Gly Trp Arg Tyr Arg Glu Val Trp Arg Pro	
995 1000 1005	
gtt tgc ggc ggt ggt gta ggg ggg ctg tgc ggc gcg tgg ctg gtg gtg	3072
Val Ser Gly Gly Gly Val Gly Gly Leu Ser Gly Ala Trp Leu Val Val	
1010 1015 1020	
tcc gag ggc gag gcg ggc ccg gtt gat gtg gtg gcg gag ggg ttg gag	3120
Ser Glu Gly Glu Ala Gly Pro Val Asp Val Val Ala Glu Gly Leu Glu	
1025 1030 1035 1040	
cgg tgt ggg gcg cga gtg gtt ccg gtg gag gtg gaa gcg ggg tgt gtg	3168
Arg Cys Gly Ala Arg Val Val Arg Val Glu Val Glu Ala Gly Cys Val	
1045 1050 1055	
agc agg gaa gtg ttg gcc ggc cac ctg cgt gag gcg gtc gat ggt gag	3216
Ser Arg Glu Val Leu Ala Gly His Leu Arg Glu Ala Val Asp Gly Glu	
1060 1065 1070	

gct gtc ggc ggt gtc gtc tcc ctt gtg ggc tgg ggg agt ggc gtc gtg Ala Val Gly Gly Val Val Ser Leu Val Gly Trp Gly Ser Gly Val Val 1075 1080 1085	3264
cag gcg gga gtg gcg tct gtg ggg ttg gtg cag gcg ctg ggt gat gtg Gln Ala Gly Val Ala Ser Val Gly Leu Val Gln Ala Leu Gly Asp Val 1090 1095 1100	3312
ggc gtg ggg gcg cgg ctg tgg tgt gtg acg ggc ggg gcc gtg tcg gtg Gly Val Gly Ala Arg Leu Trp Cys Val Thr Gly Gly Ala Val Ser Val 1105 1110 1115 1120	3360
ggg ggc cgg gat gct gtg tgg ggg ccg gcc tcg ggt gtg gtg tgg ggg Gly Gly Arg Asp Ala Val Trp Gly Pro Ala Ser Gly Val Val Trp Gly 1125 1130 1135	3408
ctg ggc cgt gtg gtg ggg gcg gag gca ccg gac cgc tgg ggt ggg ctg Leu Gly Arg Val Val Gly Ala Glu Ala Pro Asp Arg Trp Gly Gly Leu 1140 1145 1150	3456
gtt gat gtg ccg gag ctc gtg gat gag cgg gtg gtc gat ggg ttg gta Val Asp Val Pro Glu Leu Val Asp Glu Arg Val Val Asp Gly Leu Val 1155 1160 1165	3504
ggt gtg ctg gcg ggt gtg ggg gga ggg ggt gag agt gag ttt gcc gtg Gly Val Leu Ala Gly Val Gly Gly Gly Gly Glu Ser Glu Phe Ala Val 1170 1175 1180	3552
cgg tct tcg ggg gcg ttt gtg cgg cgg ttg gtg cgg gcg ccg ttg gag Arg Ser Ser Gly Ala Phe Val Arg Arg Leu Val Arg Ala Pro Leu Glu 1185 1190 1195 1200	3600
gag gcc gtc gcg gag cgg gag tgg cgg ccc cgc ggc acc gta ctc gtc Glu Ala Val Ala Glu Arg Glu Trp Arg Pro Arg Gly Thr Val Leu Val 1205 1210 1215	3648
acc gga ggc acc ggc gag ttg ggt gcg cac gtc gcc cgg tgg atg gcc Thr Gly Gly Thr Gly Glu Leu Gly Ala His Val Ala Arg Trp Met Ala 1220 1225 1230	3696
cgg cgt ggc gcc gaa cac ctg ctg ctg gtg agc cga cgc ggg gag agc Arg Arg Gly Ala Glu His Leu Leu Leu Val Ser Arg Arg Gly Glu Ser 1235 1240 1245	3744
gcc cag gga gtc gaa gaa ctc cga gcg gac ttg atg ggc ttg ggc gcg Ala Gln Gly Val Glu Glu Leu Arg Ala Asp Leu Met Gly Leu Gly Ala 1250 1255 1260	3792
cgg gtg tcg gtg gtg gcg tgt gat gcg gcg gac cgt gag gcg ttg gcg Arg Val Ser Val Val Ala Cys Asp Ala Ala Asp Arg Glu Ala Leu Ala 1265 1270 1275 1280	3840
gag gtg ttg cgg tcg gcc gtt ccg gcg gag tgc ccg ctg ggt gtg gtg Glu Val Leu Arg Ser Ala Val Pro Ala Glu Cys Pro Leu Gly Val Val 1285 1290 1295	3888
gtg cat gcc gcg gga gtt gtg gat gac ggg gtg ttg gag ggg ttg tcg Val His Ala Ala Gly Val Val Asp Asp Gly Val Leu Glu Gly Leu Ser 1300 1305 1310	3936

tcc gag cgt gtc acg ggg gtg ctg cgg gcg aag gcg ctg gcg gcc tgg	3984
Ser Glu Arg Val Thr Gly Val Leu Arg Ala Lys Ala Leu Ala Ala Trp	
1315 1320 1325	
aat ctg cat gag ttg acg cgg ggg gcg gat ctt tcg ggg ttc gtg gtg	4032
Asn Leu His Glu Leu Thr Arg Gly Ala Asp Leu Ser Gly Phe Val Val	
1330 1335 1340	
ttc tcg tcg gct gcg gcg acg ttc ggg ccg gcg gga cag ggg agt tac	4080
Phe Ser Ser Ala Ala Ala Thr Phe Gly Pro Ala Gly Gln Gly Ser Tyr	
1345 1350 1355 1360	
gcg gcg gcg aac gcg tat gtg gag gca atc gtt cgg cac cgg cgt ggt	4128
Ala Ala Ala Asn Ala Tyr Val Glu Ala Ile Val Arg His Arg Arg Gly	
1365 1370 1375	
gag ggc ctg ccg ggg ttg gcg gtg gcg tgg ggt ccg tgg gct ggt ggg	4176
Glu Gly Leu Pro Gly Leu Ala Val Ala Trp Gly Pro Trp Ala Gly Gly	
1380 1385 1390	
ggg atg gcg gag ggg gcc gtg ggg cag atg cgg cgt cgg ggt ctg gcg	4224
Gly Met Ala Glu Gly Ala Val Gly Gln Met Arg Arg Arg Gly Leu Ala	
1395 1400 1405	
gcg atg acg ccg gag acg gcg ctg gtg gca ctg ggc cag gcg ttg gac	4272
Ala Met Thr Pro Glu Thr Ala Leu Val Ala Leu Gly Gln Ala Leu Asp	
1410 1415 1420	
cat gac gag acc tgt gtg acg gtc gcc gac atc gac tgg gac cga ttc	4320
His Asp Glu Thr Cys Val Thr Val Ala Asp Ile Asp Trp Asp Arg Phe	
1425 1430 1435 1440	
acc gcc aac tcc ctc ccc ggc tcc cga ctc tcg ccc ctc atc agc gac	4368
Thr Ala Asn Ser Leu Pro Gly Ser Arg Leu Ser Pro Leu Ile Ser Asp	
1445 1450 1455	
atc ccc gaa gca cgc ctc gcc cgg gaa acc acc gga ctc gac acc gcc	4416
Ile Pro Glu Ala Arg Leu Ala Arg Glu Thr Thr Gly Leu Asp Thr Ala	
1460 1465 1470	
acc gca tcc ccc gac tcg ttc tcc gca cgg ctc aag gcc atg gac acc	4464
Thr Ala Ser Pro Asp Ser Phe Ser Ala Arg Leu Lys Ala Met Asp Thr	
1475 1480 1485	
gcc gag cag gaa cgt gcg ctt ctc gac ctg gtc cgt acg tac gcg gcg	4512
Ala Glu Gln Glu Arg Ala Leu Leu Asp Leu Val Arg Thr Tyr Ala Ala	
1490 1495 1500	
acc gtg ctc gga cac agc acc ccc acc gcc gta cgc cct gag cga gcc	4560
Thr Val Leu Gly His Ser Thr Pro Thr Ala Val Arg Pro Glu Arg Ala	
1505 1510 1515 1520	
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Phe Arg Asp Leu Gly Phe Val Ser Val Ser Ala Val Glu Leu Arg Asn	
1525 1530 1535	
cgc ctc aac gcc gtc acc ggg ctc ctc ctg ccc acc acg ctg atc ttc	4656
Arg Leu Asn Ala Val Thr Gly Leu Leu Leu Pro Thr Thr Leu Ile Phe	
1540 1545 1550	

gac tac ccc act ccc tcc gcg ctg gcc gga tac ctc aag gaa cag ctg	4704
Asp Tyr Pro Thr Pro Ser Ala Leu Ala Gly Tyr Leu Lys Glu Gln Leu	
1555 1560 1565	
gag gag ggc gcg ggc ggc cag cgt gac att gct cct ccg gtc ccg gcg	4752
Glu Glu Gly Ala Gly Gly Gln Arg Asp Ile Ala Pro Pro Val Pro Ala	
1570 1575 1580	
tcg cgt gtc gac gtt gac gag ccg att gcg att gtg ggg atg gcg tgc	4800
Ser Arg Val Asp Val Asp Glu Pro Ile Ala Ile Val Gly Met Ala Cys	
1585 1590 1595 1600	
cgt ttt ccg ggg ggt gtg gag tcg gcg gag gac ttg tgg gaa ctg gtc	4848
Arg Phe Pro Gly Gly Val Glu Ser Ala Glu Asp Leu Trp Glu Leu Val	
1605 1610 1615	
gcg tcg ggt cgg gat gcg gtg gga gag ttt ccg gtc gac cgg ggt tgg	4896
Ala Ser Gly Arg Asp Ala Val Gly Glu Phe Pro Val Asp Arg Gly Trp	
1620 1625 1630	
gac gtg gag gct ttc tat gat ccg gag ccg ggg ccg gcg ggt tcg tcg	4944
Asp Val Glu Ala Phe Tyr Asp Pro Glu Pro Gly Arg Ala Gly Ser Ser	
1635 1640 1645	
tat acg cgc cgg ggc ggt ttc ctg gag ggt gcg gcg gag ttc gat gcg	4992
Tyr Thr Arg Arg Gly Gly Phe Leu Glu Gly Ala Ala Glu Phe Asp Ala	
1650 1655 1660	
ggg ttt ttc ggg atc agt ccg cgt gag gcg ttg gcg atg gat ccg cag	5040
Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln	
1665 1670 1675 1680	
cag ccg ttg atg ctg gag gtg tcc tgg gag gcg ttg gag ccg gcg ggc	5088
Gln Arg Leu Met Leu Glu Val Ser Trp Glu Ala Leu Glu Arg Ala Gly	
1685 1690 1695	
atc gac ccc gcc acg ttg cgc ggg tcc acg acc ggt gtc ttc gcc ggc	5136
Ile Asp Pro Ala Thr Leu Arg Gly Ser Thr Thr Gly Val Phe Ala Gly	
1700 1705 1710	
atg tgc agt cag gac tac gcc gac ctc gtg cgc ccg gcc acc gag gac	5184
Met Cys Ser Gln Asp Tyr Ala Asp Leu Val Arg Arg Ala Thr Glu Asp	
1715 1720 1725	
ctc gag ggc tac gcc atg acg ggc ctg tcc agc agc gtc aca tcc gga	5232
Leu Glu Gly Tyr Ala Met Thr Gly Leu Ser Ser Ser Val Thr Ser Gly	
1730 1735 1740	
cgc gtc gcc tac acc ctg ggg ctc gag ggt ccg gcg gtg acg gtg gat	5280
Arg Val Ala Tyr Thr Leu Gly Leu Glu Gly Pro Ala Val Thr Val Asp	
1745 1750 1755 1760	
acg gcg tgt tcg tcg tcg ttg gtg gcg ctg cat ctg gcg tgt cag gcg	5328
Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala	
1765 1770 1775	
ttg agg tcg ggg gag tgt tcg ctg gcg ttg gcg ggg ggt gtg acg gtg	5376
Leu Arg Ser Gly Glu Cys Ser Leu Ala Leu Ala Gly Gly Val Thr Val	
1780 1785 1790	

atg tcg acg ccg ggt gcg ttt gtg gag ttc tcg cgg cag ccg ggt ctg	5424
Met Ser Thr Pro Gly Ala Phe Val Glu Phe Ser Arg Gln Arg Gly Leu	
1795 1800 1805	
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Ser Pro Asp Gly Arg Cys Lys Ala Tyr Gly Ser Gly Ala Asp Gly Val	
1810 1815 1820	
ggc tgg gcc gag ggt gtg ggt gtg ctg ttg gtg gag ccg ctg tcc gag	5520
Gly Trp Ala Glu Gly Val Gly Val Leu Leu Val Glu Arg Leu Ser Glu	
1825 1830 1835 1840	
gct gaa cgt cgt ggt cat ccg gtt ttg gcg gtg gtg ccg ggg agt gcg	5568
Ala Glu Arg Arg Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala	
1845 1850 1855	
gtg aat cag gac ggt gcg tcg aat ggg ttg acg gcg ccg aat ggt ccg	5616
Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro	
1860 1865 1870	
tcg cag cag ccg gtg att ccg cag gcg ttg gcg tgt gcg ggg ttg tcc	5664
Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Cys Ala Gly Leu Ser	
1875 1880 1885	
gtg gcg gat gtg gat gtg gtg gag ggg cac ggg acg ggt acg acg ttg	5712
Val Ala Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr Thr Leu	
1890 1895 1900	
ggt gat ccg atc gag gcg cag gcg ttg ctc gcc act tat ggg cag ggt	5760
Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Gly	
1905 1910 1915 1920	
cgt tcg ggg gag ccg ccg gtg tgg ttg ggg tcg gtg aag tcg aac atc	5808
Arg Ser Gly Glu Arg Pro Val Trp Leu Gly Ser Val Lys Ser Asn Ile	
1925 1930 1935	
ggg cat gcg cag gct gct gcg ggt gtg gcg ggt gtg atc aag atg gtg	5856
Gly His Ala Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val	
1940 1945 1950	
atg gcg ttg ccg gcg ggg gtg ttg ccg ccg acg ttg cat gtg gat gag	5904
Met Ala Leu Arg Ala Gly Val Leu Pro Arg Thr Leu His Val Asp Glu	
1955 1960 1965	
ccg tcg tcg cag gtg gat tgg tcg agt ggg tcg gtt cgt gtg ttg gcg	5952
Pro Ser Ser Gln Val Asp Trp Ser Ser Gly Ser Val Arg Val Leu Ala	
1970 1975 1980	
gat gag gtg gag tgg ccg ggg gtg gag ggt ccg ctg ccg cgt gcg ggg	6000
Asp Glu Val Glu Trp Pro Gly Val Glu Gly Arg Leu Arg Arg Ala Gly	
1985 1990 1995 2000	
gtg tct gcg ttc ggg gtg agt ggg acg aat gcg cat gtg att ttg gag	6048
Val Ser Ala Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu	
2005 2010 2015	
gag gcg tcc ggg ggc gcg gat ggg ggt gcg ggc ccg ctg cag gag ttg	6096
Glu Ala Ser Gly Gly Ala Asp Gly Gly Ala Gly Arg Leu Gln Glu Leu	
2020 2025 2030	

ggt Gly	ccg Pro	ggg Gly 2035	gtg Val	gtg Val	tcg Ser	ggt Gly 2040	tcg Ser	ggg Gly	gtg Val	gtg Val	ccg Pro	tgg Trp 2045	gtg Val	gtg Val	tcg Ser	6144
gcg Ala 2050	cgg Arg	tcg Ser	gag Glu	ttg Leu	gcg Ala 2055	ttg Leu	cgg Arg	ggg Gly	cag Gln	gcg Ala 2060	cgt Arg	cgg Arg	ttg Leu	cgt Arg	ggg Gly	6192
gtt Val 2065	gtg Val	gcg Ala	gtt Val	ggt Gly 2070	ggg Gly	ggt Gly	gcg Ala	gat Asp	ggg Gly	gtg Val 2075	ggg Gly	gtg Val	agt Ser	ccg Pro	gct Ala 2080	6240
ggg Gly	gtc Val	ggg Gly	cgg Arg 2085	gct Ala	ttg Leu	gtg Val	tcg Ser	gag Glu 2090	cgg Arg	tcg Ser	gtg Val	ttc Phe	gag Glu 2095	cat His	cgt Arg	6288
gcg Ala	gtg Val	gtc Val 2100	gtg Val	gcc Ala	gag Glu	gac Asp	cgc Arg 2105	gac Asp	gag Glu	ttc Phe	ctg Leu	cac His 2110	gca Ala	ctc Leu	gac Asp	6336
gca Ala 2115	ctg Leu	gcc Ala	gag Glu	ggg Gly	gca Ala	ccc Pro 2120	acc Thr	gcg Ala	ggg Gly	gtg Val	gta Val 2125	cag Gln	ggt Gly	gtg Val	gcc Ala	6384
gga Gly 2130	ccg Pro	gcg Ala	gcc Ala	gac Asp	gga Gly 2135	aag Lys	atc Ile	gcc Ala	atg Met	ctg Leu 2140	ttc Phe	gga Gly	gga Gly	cag Gln	ggc Gly	6432
acc Thr 2145	cac His	tgg Trp	gaa Glu	ggc Gly 2150	atg Met	gcg Ala	cag Gln	gaa Glu	ctc Leu 2155	ctc Leu	ggc Gly	tcc Ser	tca Ser	ccg Pro	gtc Val 2160	6480
ttc Phe	gcc Ala	cag Gln 2165	cag Gln	atg Met	tcc Ser	gac Asp	tgc Cys	gcc Ala 2170	caa Gln	gcc Ala	ctc Leu 2205	gaa Glu	ccg Pro	tac Tyr 2175	ctg Leu	6528
gac Asp	tgg Trp	tct Ser 2180	ctc Leu	ctc Leu	gac Asp	gtc Val	ctg Leu 2185	cgc Arg	ggc Gly	gca Ala	ccg Pro	gac Asp 2190	gca Ala	ccc Pro	cct Pro	6576
ctg Leu	caa Gln 2195	cgc Arg	gtc Val	gat Asp	gtc Val	gtc Val 2200	cag Gln	ccc Pro	gtc Val	ctc Leu	ttc Phe 2205	gcg Ala	gtg Val	atg Met	gtc Val	6624
tcg Ser 2210	ctg Leu	gcg Ala	gcg Ala	ctc Leu	tgg Trp 2215	cgc Arg	tcg Ser	tac Tyr	ggt Gly	gta Val 2220	cac His	ccg Pro	gac Asp	gcg Ala	gtg Val	6672
gcc Ala 2225	ggg Gly	cac His	tcg Ser	cag Gln 2230	ggc Gly	gag Glu	atc Ile	gca Ala	gcg Ala 2235	gcc Ala	tac Tyr	gtc Val	gcc Ala	ggt Gly 2240	gca Ala	6720
ctc Leu	tcc Ser	ctc Leu	gac Asp 2245	gac Asp	gcc Ala	gcc Ala	cgg Arg	gtc Val 2250	acc Thr	gcc Ala	ctg Leu	cgc Arg	agc Ser 2255	cag Gln	gcg Ala	6768
ctg Leu	gcc Ala	gca Ala 2260	ctg Leu	gcc Ala	ggg Gly	cag Gln	ggg Gly 2265	gcg Ala	atg Met	gca Ala	tcg Ser 2270	gtc Val	ggt Gly	ctg Leu	ccg Pro	6816

gtc gag aag ctg gag ccg cgt ctt gcg aca tgg ggc gac cgt ctg gtc Val Glu Lys Leu Glu Pro Arg Leu Ala Thr Trp Gly Asp Arg Leu Val 2275 2280 2285	6864
atc gcc gcc gtg aac ggg gcg cgt tgc gcc gtg gtc tcc ggg gag ccg Ile Ala Ala Val Asn Gly Ala Arg Ser Ala Val Val Ser Gly Glu Pro 2290 2295 2300	6912
gaa gcg gtc gac gcc ctg gtg gag gag ctg tca cac gaa gac gta ccg Glu Ala Val Asp Ala Leu Val Glu Glu Leu Ser His Glu Asp Val Pro 2305 2310 2315 2320	6960
gcc cgc agg ctc atg gtc gac tgg gcg tgc cac tcc ccg cag gtc gag Ala Arg Arg Leu Met Val Asp Trp Ala Ser His Ser Pro Gln Val Glu 2325 2330 2335	7008
gcg atc cag ggg cgg ctg ctc gaa ctc ctc gcc ccc atc cgc gcg agg Ala Ile Gln Gly Arg Leu Leu Glu Leu Leu Ala Pro Ile Arg Ala Arg 2340 2345 2350	7056
acc ggc gac gtg ccc ttc tac tcc acc gtc acc ggc gaa cgc atc gac Thr Gly Asp Val Pro Phe Tyr Ser Thr Val Thr Gly Glu Arg Ile Asp 2355 2360 2365	7104
ggc acc gaa ctc gac gcc gac tac tgg tac cgc aac ctg cgc cag gtc Gly Thr Glu Leu Asp Ala Asp Tyr Trp Tyr Arg Asn Leu Arg Gln Val 2370 2375 2380	7152
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gtc ttc atc gag gcg tgc ccg cat ccg gcc gtc gcg gtc ggt gtg cag Val Phe Ile Glu Ala Cys Pro His Pro Ala Val Ala Val Gly Val Gln 2405 2410 2415	7248
gaa acc ctg gac gag atg ggt gac ttg gac agc ctg gtc gtc gga tct Glu Thr Leu Asp Glu Met Gly Asp Leu Asp Ser Leu Val Val Gly Ser 2420 2425 2430	7296
ctg cgc cgg ggc gaa ggc ggc ttg cga cgc ttc ctg atg tcc gtg gcc Leu Arg Arg Gly Glu Gly Gly Leu Arg Arg Phe Leu Met Ser Val Ala 2435 2440 2445	7344
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tat gcg ttc gag cga gag cgc ttt tgg ctg gat gtg gag ggg gcg ccg Tyr Ala Phe Glu Arg Glu Arg Phe Trp Leu Asp Val Glu Gly Ala Pro 2485 2490 2495	7488
cgg ggt tcc ggg gtc tct ggg cag tgg ggt ggt cag ttg tgc gag gcg Arg Gly Ser Gly Val Ser Gly Gln Trp Gly Gly Gln Leu Ser Glu Ala 2500 2505 2510	7536

gtg gac acc gtg cgc ggc ggc atg ctg cgc gac tgc ctc gcc gga ctc	7584
Val Asp Thr Val Arg Gly Gly Met Leu Arg Asp Cys Leu Ala Gly Leu	
2515 2520 2525	
gac ccc gcc gca cag gcc gag acc gtg ctg gac ctg gtc ctt acc cat	7632
Asp Pro Ala Ala Gln Ala Glu Thr Val Leu Asp Leu Val Leu Thr His	
2530 2535 2540	
gcc gcg gcc gtc ctt gga cac ggc acc gcc gat gcg gtg gtg ccc gag	7680
Ala Ala Ala Val Leu Gly His Gly Thr Ala Asp Ala Val Val Pro Glu	
2545 2550 2555 2560	
cgc gcc ttc cgc gac ctc ggt ttc gac tcc ctc acc gcc gtc gaa cta	7728
Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu	
2565 2570 2575	
cgc aac cgc ctc aac acc gcc acg ggc ctg cgc ttc ccg agg acc ctg	7776
Arg Asn Arg Leu Asn Thr Ala Thr Gly Leu Arg Phe Pro Arg Thr Leu	
2580 2585 2590	
gtg ttc gac cat ccc cgc ccg gtg gca ctc gcg gca cac atc cac gag	7824
Val Phe Asp His Pro Arg Pro Val Ala Leu Ala Ala His Ile His Glu	
2595 2600 2605	
cag ctg agc ggc gga agc ccg acc acc ggc act gcc ctt gcc ctt gcc	7872
Gln Leu Ser Gly Gly Ser Pro Thr Thr Gly Thr Ala Leu Ala Leu Ala	
2610 2615 2620	
ctt cgg gcc ccg gca ccg cgt gtg gat gtc gac gag ccg att gcc att	7920
Leu Arg Ala Pro Ala Pro Arg Val Asp Val Asp Glu Pro Ile Ala Ile	
2625 2630 2635 2640	
gtg ggg atg gcg tgc cgt ttt ccg ggg ggt gtg gag tgc gcg gag gat	7968
Val Gly Met Ala Cys Arg Phe Pro Gly Gly Val Glu Ser Ala Glu Asp	
2645 2650 2655	
ttc tgg gag ttg atc gcg tgc ggt cgg gat gcg gtg ggg gag ttt ccg	8016
Phe Trp Glu Leu Ile Ala Ser Gly Arg Asp Ala Val Gly Glu Phe Pro	
2660 2665 2670	
gtc gac cgg ggt tgg gac gtg gag gct ttc tat gat ccg gag ccg ggg	8064
Val Asp Arg Gly Trp Asp Val Glu Ala Phe Tyr Asp Pro Glu Pro Gly	
2675 2680 2685	
cgg gcg ggt acg tcc tac acg cgg tgt ggt ggg ttt ttg cag ggt gcg	8112
Arg Ala Gly Thr Ser Tyr Thr Arg Cys Gly Gly Phe Leu Gln Gly Ala	
2690 2695 2700	
gcg gag ttc gat gcg ggg ttt ttc ggg atc agt ccg cgt gag gcg ttg	8160
Ala Glu Phe Asp Ala Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu	
2705 2710 2715 2720	
gcg atg gat ccg cag cag cgg ttg atg ctg gag gtg tcc tgg gag gcg	8208
Ala Met Asp Pro Gln Gln Arg Leu Met Leu Glu Val Ser Trp Glu Ala	
2725 2730 2735	
ttg gag cgg gcg ggc atc gac ccc gcc acg ctg cac ggg tcc acg acc	8256
Leu Glu Arg Ala Gly Ile Asp Pro Ala Thr Leu His Gly Ser Thr Thr	
2740 2745 2750	

ggt	gtc	ttc	gcc	ggc	gtc	tcg	cag	cag	gac	tac	gcc	gag	ctc	ctg	cgc	8304
Gly	Val	Phe	Ala	Gly	Val	Ser	Gln	Gln	Asp	Tyr	Ala	Glu	Leu	Leu	Arg	
2755						2760			2765							
cgc	ggc	acc	cag	gac	cac	gag	ggg	tac	gcg	ctc	acc	ggc	gtc	tcc	aac	8352
Arg	Gly	Thr	Gln	Asp	His	Glu	Gly	Tyr	Ala	Leu	Thr	Gly	Val	Ser	Asn	
2770						2775			2780							
agc	gtc	gtc	tcc	ggg	cgg	ctt	tcc	tac	acc	ttc	ggc	ttc	gag	ggt	cgc	8400
Ser	Val	Val	Ser	Gly	Arg	Leu	Ser	Tyr	Thr	Phe	Gly	Phe	Glu	Gly	Pro	
2785			2790						2795			2800				
gcg	gtg	acg	gtg	gat	acg	gcg	tgt	tcg	tcg	tcg	ttg	gtg	gcg	ctg	cat	8448
Ala	Val	Thr	Val	Asp	Thr	Ala	Cys	Ser	Ser	Ser	Leu	Val	Ala	Leu	His	
			2805						2810			2815				
ctg	gcg	tgt	cag	gcg	ttg	agg	tcg	ggg	gag	tgt	tcg	ctg	gcg	ttg	gcg	8496
Leu	Ala	Cys	Gln	Ala	Leu	Arg	Ser	Gly	Glu	Cys	Ser	Leu	Ala	Leu	Ala	
			2820			2825						2830				
ggg	ggt	gtg	acg	gtg	atg	tcg	acg	ccg	ggt	gcg	ttt	gtg	gag	ttc	tcg	8544
Gly	Gly	Val	Thr	Val	Met	Ser	Thr	Pro	Gly	Ala	Phe	Val	Glu	Phe	Ser	
2835						2840			2845							
cgg	cag	cgg	ggt	ctg	tcg	ccg	gac	ggc	cgg	tgc	aag	gcg	tac	ggg	tcg	8592
Arg	Gln	Arg	Gly	Leu	Ser	Pro	Asp	Gly	Arg	Cys	Lys	Ala	Tyr	Gly	Ser	
2850						2855			2860							
ggg	gcc	gat	ggg	gtc	ggc	tgg	gcc	gag	ggt	gtg	ggt	gtg	ctg	ttg	gtg	8640
Gly	Ala	Asp	Gly	Val	Gly	Trp	Ala	Glu	Gly	Val	Gly	Val	Leu	Leu	Val	
2865			2870						2875			2880				
gag	cgg	ctg	tcc	gag	gct	gaa	cgt	cgt	ggt	cat	cgg	gtt	ttg	gcg	gtg	8688
Glu	Arg	Leu	Ser	Glu	Ala	Glu	Arg	Arg	Gly	His	Arg	Val	Leu	Ala	Val	
			2885						2890			2895				
gtg	cgg	ggg	agt	gcg	gtg	aat	cag	gac	ggt	gcg	tcg	aat	ggg	ttg	acg	8736
Val	Arg	Gly	Ser	Ala	Val	Asn	Gln	Asp	Gly	Ala	Ser	Asn	Gly	Leu	Thr	
2900						2905			2910							
gcg	ccg	aat	ggt	ccg	tcg	cag	cag	cgg	gtg	att	cgg	cag	gcg	ttg	gcg	8784
Ala	Pro	Asn	Gly	Pro	Ser	Gln	Gln	Arg	Val	Ile	Arg	Gln	Ala	Leu	Ala	
2915						2920			2925							
tgt	gcg	ggg	ttg	tcc	gtg	gcg	gat	gtg	gat	gtg	gtg	gag	ggg	cac	ggg	8832
Cys	Ala	Gly	Leu	Ser	Val	Ala	Asp	Val	Asp	Val	Val	Glu	Gly	His	Gly	
2930			2935						2940							
acg	ggt	acg	acg	ttg	ggt	gat	ccg	atc	gag	gcg	cag	gcg	ttg	ctc	gcc	8880
Thr	Gly	Thr	Thr	Leu	Gly	Asp	Pro	Ile	Glu	Ala	Gln	Ala	Leu	Leu	Ala	
2945			2950						2955			2960				
acg	tac	ggg	cag	ggt	cgt	tcg	ggg	gag	cgg	ccg	gtg	tgg	ttg	ggg	tcg	8928
Thr	Tyr	Gly	Gln	Gly	Arg	Ser	Gly	Glu	Arg	Pro	Val	Trp	Leu	Gly	Ser	
			2965			2970			2975							
gtg	aag	tcg	aac	atc	ggg	cat	gcg	cag	gct	gcc	gcg					

gtg atc aag atg gtc atg gcc ctg aac cac gaa ctg ttg ccg acc agc	9024
Val Ile Lys Met Val Met Ala Leu Asn His Glu Leu Leu Pro Thr Ser	
2995 3000 3005	
ctg cac atc gac gaa ccc tcc ccc cac atc gac tgg tcg agc ggc ggc	9072
Leu His Ile Asp Glu Pro Ser Pro His Ile Asp Trp Ser Ser Gly Gly	
3010 3015 3020	
gtc cgg ctt ctc acc gag ccc gta ccg tgg cag cag aac ggc cgg ccc	9120
Val Arg Leu Leu Thr Glu Pro Val Pro Trp Gln Gln Asn Gly Arg Pro	
3025 3030 3035 3040	
agg cgc gcg ggc gtc tcc gcg ttc gga gtc agc ggg acc aac gcc cac	9168
Arg Arg Ala Gly Val Ser Ala Phe Gly Val Ser Gly Thr Asn Ala His	
3045 3050 3055	
gtc atc atc gag cag gcg ccg gtc gag gcg cac gtc atc agt gag ccg	9216
Val Ile Ile Glu Gln Ala Pro Val Glu Ala His Val Ile Ser Glu Pro	
3060 3065 3070	
gta ccg gct gag gcg cac gtc atc gtc gag cag gcg ccg gtc gag gcg	9264
Val Pro Ala Glu Ala His Val Ile Val Glu Gln Ala Pro Val Glu Ala	
3075 3080 3085	
ccc cac gtg gtc gac gcc acc gga ccg gcg gac ctc acc gag ccg caa	9312
Pro His Val Val Asp Ala Thr Gly Pro Ala Asp Leu Thr Glu Pro Gln	
3090 3095 3100	
gag gag gcg gct gaa ccg gag tgc gtc gct gac gcc gtg acc gag atg	9360
Glu Glu Ala Ala Glu Pro Glu Cys Val Ala Asp Ala Val Thr Glu Met	
3105 3110 3115 3120	
tcg gct gaa ccg gag tgc gtc gcc gac gcc atg tcc gag atg tcg gct	9408
Ser Ala Glu Pro Glu Cys Val Ala Asp Ala Met Ser Glu Met Ser Ala	
3125 3130 3135	
gag tgc gtc gcc gag gcc gtg tcc gac aag tcg gct gaa ccg gag tgc	9456
Glu Cys Val Ala Glu Ala Val Ser Asp Lys Ser Ala Glu Pro Glu Cys	
3140 3145 3150	
gtc gcc gac gcc atg tcc gac aag ccg gcc ctc ctg ccc atc ccg tgg	9504
Val Ala Asp Ala Met Ser Asp Lys Pro Ala Leu Leu Pro Ile Pro Trp	
3155 3160 3165	
ctg ctc tcc gcc aag tcc gag cga gcg ctg cgg ggc cag gcg cga cgg	9552
Leu Leu Ser Ala Lys Ser Glu Arg Ala Leu Arg Gly Gln Ala Arg Arg	
3170 3175 3180	
ttg cgg cag ttc gct gcc agg gca tcc gat gcc cgg ccg gcc gac gtg	9600
Leu Arg Gln Phe Ala Ala Arg Ala Ser Asp Ala Arg Pro Ala Asp Val	
3185 3190 3195 3200	
gcg cac gcc ctg gcg gca cag cgg tcc gtg ttc gat cac cgg gcc gtc	9648
Ala His Ala Leu Ala Ala Gln Arg Ser Val Phe Asp His Arg Ala Val	
3205 3210 3215	
gtc gtg gcc gag gac cgc gac ggc ttc ctt cag gcc ctc gac gcg ctg	9696
Val Val Ala Glu Asp Arg Asp Gly Phe Leu Gln Ala Leu Asp Ala Leu	
3220 3225 3230	

gcc gag ggc cgg tcg gcg gac ggc ctg atc gaa ggg tcg gtc ggc ccg	9744
Ala Glu Gly Arg Ser Ala Asp Gly Leu Ile Glu Gly Ser Val Gly Pro	
3235 3240 3245	
cgt ggc ggc cac tca ggc cgc cgg cgc gga aag acc gcc atg ctg ttc	9792
Arg Gly Gly His Ser Gly Arg Arg Arg Gly Lys Thr Ala Met Leu Phe	
3250 3255 3260	
gcc gga cag ggc acg caa cgc gtg gga atg ggc cgt cag ctg tat gcg	9840
Ala Gly Gln Gly Thr Gln Arg Val Gly Met Gly Arg Gln Leu Tyr Ala	
3265 3270 3275 3280	
gct cac ccg gcc tac gcg gac gcg ctg gac cag gta ctg gcg gaa ctg	9888
Ala His Pro Ala Tyr Ala Asp Ala Leu Asp Gln Val Leu Ala Glu Leu	
3285 3290 3295	
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Asp Gly His Leu Asp Gln Pro Leu Arg Pro Leu Ile His Ala Ser Ala	
3300 3305 3310	
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Asp Leu Ala Asp Val Ala Asp Ala Ala Asp Val Leu Asp Arg Thr Arg	
3315 3320 3325	
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Tyr Ala Gln Pro Ala Leu Phe Ala Val Gln Val Ala Leu Phe Arg His	
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Leu Glu Arg Leu Gly Val Arg Ala Asp Phe Val Ala Gly His Ser Ile	
3345 3350 3355 3360	
ggc gag ctc gcg gcc gcc cac gtc gcc ggg gtg ctt ccc ctg gca gca	10128
Gly Glu Leu Ala Ala Ala His Val Ala Gly Val Leu Pro Leu Ala Ala	
3365 3370 3375	
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Ala Cys Arg Leu Val Ala Ala Arg Gly Arg Leu Met Glu Gln Leu Ala	
3380 3385 3390	
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Pro Gly Gly Ala Met Val Ala Val Arg Ala Ser Glu Ala Glu Ala Arg	
3395 3400 3405	
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Gln Ala Leu Asp Gly Arg Glu Ala Arg Val Ser Val Ala Ala Val Asn	
3410 3415 3420	
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Gly Pro Ala Ser Val Val Phe Ser Gly Ala Glu Asp Glu Val Gly Asn	
3425 3430 3435 3440	
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Met Ala Asp Trp Phe Ala Glu Arg Gly Arg Arg Val Lys Arg Leu Arg	
3445 3450 3455	
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Thr Gly His Ala Phe His Ser Pro Leu Met Asp Pro Met Leu Glu Glu	
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Phe Gln Gln Val Ala Ala Ser Leu Thr Tyr Ser Glu Pro Ala Ile Pro	
3475 3480 3485	
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Met Val Ser Thr Leu Thr Gly Asp Ile Val Ala Ala Gly Glu Leu Ser	
3490 3495 3500	
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Asp Pro Glu Tyr Trp Val Arg Gln Val Arg Arg Thr Val Arg Phe Gly	
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Asp Ala Ile Ser Arg Leu His Thr Asp Gly Val Arg Thr Phe Met Glu	
3525 3530 3535	
ctg ggc cca gac ggg acc ctg tcg gca ctg gcc gag gaa tgc cta gag	10656
Leu Gly Pro Asp Gly Thr Leu Ser Ala Leu Ala Glu Glu Cys Leu Glu	
3540 3545 3550	
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Ala Thr Ala Asp Ser His Pro Ala Asp Asp Asp Thr Gly Thr Pro Gln	
3555 3560 3565	
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Glu Asn Leu Leu Ile Pro Leu Leu Arg Pro Asp Ser Pro Glu Pro Gly	
3570 3575 3580	
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Thr Leu Leu Thr Gly Leu Ala Arg Leu His Thr His Gly Ala Ala Ala	
3585 3590 3595 3600	
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Val Asn Trp Pro Ala Ala Leu Pro Glu Arg Asp Arg Ala Arg His Leu	
3605 3610 3615	
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Asp Leu Pro Thr Tyr Ala Phe Asp His His Arg Tyr Trp Val Asp Thr	
3620 3625 3630	
tcg gcc ggc cac ccg ggg gac ctg tcg gca gcg ggg ctc ggc acc gcc	10944
Ser Ala Gly His Pro Gly Asp Leu Ser Ala Ala Gly Leu Gly Thr Ala	
3635 3640 3645	
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Gly His Pro Leu Leu Gly Ser Ala Val Ala Leu Ala Glu Ser Gln Glu	
3650 3655 3660	
ctc ctc ttc acc ggc cgt ctc tcc ctg cgc aca cac ccg tgg ctg gcc	11040
Leu Leu Phe Thr Gly Arg Leu Ser Leu Arg Thr His Pro Trp Leu Ala	
3665 3670 3675 3680	
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Asp His Ala Ile Phe Gly Thr Val Leu Leu Pro Gly Thr Ala Ile Leu	
3685 3690 3695	
gaa ctg gcc gtg cgc gca ggc gac gag gtc gac tgc ggc acc gtc gag	11136
Glu Leu Ala Val Arg Ala Gly Asp Glu Val Asp Cys Gly Thr Val Glu	
3700 3705 3710	

gaa ctc acc ctg cgg aca ccg ctc gtc ctt ccc gaa cag ggc tcg gtg Glu Leu Thr Leu Arg Thr Pro Leu Val Leu Pro Glu Gln Gly Ser Val 3715 3720 3725	11184
atc ctg caa ctc tcc gtc ggg gca ccc cag ggc ccc cag acg ccc gag Ile Leu Gln Leu Ser Val Gly Ala Pro Gln Gly Pro Gln Thr Pro Glu 3730 3735 3740	11232
gag ccc gaa cgg cgc acc ttc gcc ctg tac gcc cgc gaa gac gac gga Glu Pro Glu Arg Arg Thr Phe Ala Leu Tyr Ala Arg Glu Asp Asp Gly 3745 3750 3755 3760	11280
ctg tcg tcc tcg tcc gcg gcg gcg acc ggc acc gag tgg acc tgc cac Leu Ser Ser Ser Ala Ala Ala Thr Gly Thr Glu Trp Thr Cys His 3765 3770 3775	11328
gcc acc ggc gtc ctg acc ggc acc gcc cgg ccc gcg gag gag cac aca Ala Thr Gly Val Leu Thr Gly Thr Ala Arg Pro Ala Glu Glu His Thr 3780 3785 3790	11376
cag gaa ccg tgg ccg ccc gcc gac gca gca ccg gtg gac ctg gac ggc Gln Glu Pro Trp Pro Pro Ala Asp Ala Ala Pro Val Asp Leu Asp Gly 3795 3800 3805	11424
tgg tac gag cag ctg gcc ggc gcc ggc ctg gga tac ggg ccg gtg ttc Trp Tyr Glu Gln Leu Ala Gly Ala Gly Leu Gly Tyr Gly Pro Val Phe 3810 3815 3820	11472
cag ggg ctg cgc gag gtc tgg ccg cgc ggg gac gag gtg ttc gcc gtc Gln Gly Leu Arg Glu Val Trp Arg Arg Gly Asp Glu Val Phe Ala Val 3825 3830 3835 3840	11520
gtc acc ctg ccc gag agc acg gag gga cag gcg gcc gac gcc gcc cgg Val Thr Leu Pro Glu Ser Thr Glu Gly Gln Ala Ala Asp Ala Ala Arg 3845 3850 3855	11568
tac gcc ctg cac ccg gcc ctg ctg gac gcg gca ctg cac ccg gtc gtt Tyr Ala Leu His Pro Ala Leu Leu Asp Ala Ala Leu His Pro Val Val 3860 3865 3870	11616
ctg cgc cac gag ggc gat gcc gcc gcc gac gga cac ggc tgg ctg ccg Leu Arg His Glu Gly Asp Ala Ala Ala Asp Gly His Gly Trp Leu Pro 3875 3880 3885	11664
ttc tcc tgg acc ggc gtc acg gtc gcc gcc tcc ggc gcc tcc acc ctg Phe Ser Trp Thr Gly Val Thr Val Ala Ala Ser Gly Ala Ser Thr Leu 3890 3895 3900	11712
cac gtc cgt ctc acc gtc cgc acg gac gag gac gcg gtc gga ctg ctg His Val Arg Leu Thr Val Arg Thr Asp Glu Asp Ala Val Gly Leu Leu 3905 3910 3915 3920	11760
gcc acc gac gca tcg gga cgc atc gtc atc tcc gcg ggg tcc ctc gcc Ala Thr Asp Ala Ser Gly Arg Ile Val Ile Ser Ala Gly Ser Leu Ala 3925 3930 3935	11808
ttc cgg ccc gtc tcc gcc gag cag ctc cag gcc gcg cgc acc ggc tac Phe Arg Pro Val Ser Ala Glu Gln Leu Gln Ala Ala Arg Thr Gly Tyr 3940 3945 3950	11856

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His Asp His Leu Phe Arg Ile Glu Trp Arg Pro Leu His Leu Pro Thr	
3955 3960 3965	
aca ccg gca cgg aca gcc gac tgg gcc cta atc ggc ccc ggt gcc cgg	11952
Thr Pro Ala Arg Thr Ala Asp Trp Ala Leu Ile Gly Pro Gly Ala Arg	
3970 3975 3980	
cgg acg gcc gcc gtc ctg gag cgc aac ggc gcc tcc tgg cag gcc tac	12000
Arg Thr Ala Ala Val Leu Glu Arg Asn Gly Ala Ser Trp Gln Ala Tyr	
3985 3990 3995 4000	
ccg gac ccg gcg gct ctc gca gaa gcc ctg gcg gcc ggc gcc ccg gca	12048
Pro Asp Pro Ala Ala Leu Ala Glu Ala Leu Ala Ala Gly Ala Pro Ala	
4005 4010 4015	
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Pro Gly Met Val Val Ile Ser Cys Glu Pro Asp Gly Ala Ser Ala Pro	
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acc gat tcc gcc ctc acc gat tcc gcc ctc acc gat tcc gcc ccg gcc	12144
Thr Asp Ser Ala Leu Thr Asp Ser Ala Leu Thr Asp Ser Ala Pro Ala	
4035 4040 4045	
ggc tcg gcc ccg gcc gac tcc acc gcc ctc gcc gac gcc acc cgg caa	12192
Gly Ser Ala Pro Ala Asp Ser Thr Ala Leu Ala Asp Ala Thr Arg Gln	
4050 4055 4060	
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Ala Thr Thr Arg Val Leu Ala Leu Leu Gln Glu Trp Val Ala Asp Glu	
4065 4070 4075 4080	
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Arg Leu Ala Ala Cys Arg Leu Ala Leu Leu Thr His Gly Ser Val Thr	
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Ala Thr Pro Asp Glu Pro Val Ser Asp Leu Ala His Ala Ala Val Trp	
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4130 4135 4140	
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Ala Gly Glu Pro Gln Ile Ala Leu Arg Asn Gly Ala Val Arg Ile Pro	
4145 4150 4155 4160	
cgg atg aca cga gtg ccc gtc cgg cag cca cag ccg agc acc acc gac	12528
Arg Met Thr Arg Val Pro Val Arg Gln Pro Gln Pro Ser Thr Thr Asp	
4165 4170 4175	
gcc gac tgg gac ccg gag gcc acg gtc ctc atc acg ggc ggt acc gcc	12576
Ala Asp Trp Asp Pro Glu Ala Thr Val Leu Ile Thr Gly Gly Thr Gly	
4180 4185 4190	

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Val Leu Gly Arg Leu Val Ala Arg His Leu Ala Thr Ala His Gly Val	
4195 4200 4205	
cgg cac ctg ctg ctg gcc acc cgc cgc ggc acg gcc gcg gac ggc gcc	12672
Arg His Leu Leu Leu Ala Thr Arg Arg Gly Thr Ala Ala Asp Gly Ala	
4210 4215 4220	
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Ala Asp Leu Val Ala Glu Leu Ala Gly Leu Gly Ala Glu Ala Thr Val	
4225 4230 4235 4240	
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Ala Ala Cys Asp Ile Gly Asp Arg Ala Ala Val Ala Ala Leu Leu Asp	
4245 4250 4255	
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Gln Val Pro Ala Gln His Pro Leu Lys Ala Val Ile His Thr Ala Gly	
4260 4265 4270	
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Val Val Asp Asp Gly Ile Leu Thr Ser Leu Thr Pro Glu Arg Met Glu	
4275 4280 4285	
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Ala Val Leu His Ala Lys Ala Phe Gly Ala Ala His Leu His Asp Leu	
4290 4295 4300	
acc cgc gac gcc ggc ctc acc acc ttc acc gtc ttc tcc tcg gcc gcc	12960
Thr Arg Asp Ala Gly Leu Thr Thr Phe Thr Val Phe Ser Ser Ala Ala	
4305 4310 4315 4320	
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Ala Ser Phe Gly Ser Pro Gly Gln Gly Asn Tyr Thr Ala Ala Asn Ala	
4325 4330 4335	
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Phe Leu Asp Ala Leu Met Gln His Arg His Thr Gln Ala Leu Pro Gly	
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Arg Ser Leu Ala Trp Gly Leu Trp Gly Glu Ala Asp Gly Met Thr Arg	
4355 4360 4365	
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Asn Leu Ala Gly Thr Asp Phe Ala Arg Met Ala Arg Gly Gly Leu Leu	
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Pro Leu Ser Asn Ala Gln Gly Leu Ala Leu Leu Asp Thr Ala Asp Arg	
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Leu Gly Pro Phe Gly Asp Gly Leu Leu Leu Ala Thr Arg Leu Asp Ala	
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Ala Thr Leu His Ala Gln Ala Thr Ala Gly Ala Leu Pro Arg Ile Leu	
4420 4425 4430	

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gcg acc gac acc ccc gcc acg ctg cgc gag cgc ctg gcc gga ctc acc Ala Thr Asp Thr Pro Ala Thr Leu Arg Glu Arg Leu Ala Gly Leu Thr 4450 4455 4460	13392
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gcc gcc gcc gtc ctc ggc cac ccc acc agc gcc gtc aca gcc gcg gac Ala Ala Ala Val Leu Gly His Pro Thr Ser Ala Val Thr Ala Ala Asp 4485 4490 4495	13488
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ctc ggc ttc gac tcg ctg acc gcc gtc gaa ctc cgc aac cgg atc aac Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu Arg Asn Arg Ile Asn 4515 4520 4525	13584
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agc ccc gcg gca ctc gcc gat cac ctc gcg acc cgc ctg acg gcc gag Ser Pro Ala Ala Leu Ala Asp His Leu Ala Thr Arg Leu Thr Ala Glu 4545 4550 4555 4560	13680
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ctg ttc tgg atc gga cac gac acc cgc cgc atc gag gag tcc atg gcc Leu Phe Trp Ile Gly His Asp Thr Arg Arg Ile Glu Glu Ser Met Ala 4610 4615 4620	13872
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gcc caa ggt gaa gca ctc gcc ccg ggc gaa aca ccg ccc gcc ctc atc Ala Gln Gly Glu Ala Leu Ala Arg Gly Glu Thr Arg Pro Ala Leu Ile 4660 4665 4670	14016

tgc ctg ccc acc gtc gcc gcc gtg tgc agc gtg tac cag tac tca cgt	14064
Cys Leu Pro Thr Val Ala Ala Val Ser Ser Val Tyr Gln Tyr Ser Arg	
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Phe Ala Ala Gly Leu Asn Gly His Arg Asp Val Trp Tyr Val Pro Ala	
4690 4695 4700	
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Pro Gly Phe Leu Glu Gly Glu Pro Leu Pro Ser Gly Ile Gly Ala Val	
4705 4710 4715 4720	
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Thr Arg Met Phe Ala Asp Ala Ile Val Arg Phe Thr Asp Gly Ala Pro	
4725 4730 4735	
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Phe Ala Leu Ala Gly His Ser Ala Gly Gly Trp Phe Val Tyr Ala Val	
4740 4745 4750	
acg agt cat ctg gag cgt cta ggc gtc cgt ccg gaa gcg gtg gtg acc	14304
Thr Ser His Leu Glu Arg Leu Gly Val Arg Pro Glu Ala Val Val Thr	
4755 4760 4765	
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Met Asp Ala Tyr Leu Pro Asp Asp Gly Ile Ala Pro Val Ala Ser Ala	
4770 4775 4780	
ctg aca agt gaa atc ttc gac cgc gtc acg cag ttt gtg gac gtg gac	14400
Leu Thr Ser Glu Ile Phe Asp Arg Val Thr Gln Phe Val Asp Val Asp	
4785 4790 4795 4800	
tac aca cgc ctg gtc gcc atg ggc gga tac ttc cgc atc ttc tcc ggc	14448
Tyr Thr Arg Leu Val Ala Met Gly Gly Tyr Phe Arg Ile Phe Ser Gly	
4805 4810 4815	
tgg agt cct ccg gac atc acc aca ccc gcc ctc ttc ctg cgc ggc ccg	14496
Trp Ser Pro Pro Asp Ile Thr Thr Pro Ala Leu Phe Leu Arg Gly Arg	
4820 4825 4830	
gac gga gaa cag atg ccg ccg ccg tgg gga gtt ccg cac acc gtt ctg	14544
Asp Gly Glu Gln Met Pro Pro Pro Trp Gly Val Pro His Thr Val Leu	
4835 4840 4845	
gac atc cag ggg aat cac ttc acg atg ctg gaa cag ttt gcg gat tgc	14592
Asp Ile Gln Gly Asn His Phe Thr Met Leu Glu Gln Phe Ala Asp Ser	
4850 4855 4860	
act gct ccg cat gtc gac gaa tgg ctg aca gaa atc gca tca gtg ccg	14640
Thr Ala Arg His Val Asp Glu Trp Leu Thr Glu Ile Ala Ser Val Arg	
4865 4870 4875 4880	
cgc tgcacgcgcc tctgatcgcg gtcctgatcg cgccctgat cggcgggtcg	14693
Arg	
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catcgatcag tgctttcccc cttacggcca tacgggcctt tctgagactt cttgaatttg	14813

ggagacagtg atg gac acg tcc agc gaa aag ctc gtc gac gcg ctt agg Met Asp Thr Ser Ser Glu Lys Leu Val Asp Ala Leu Arg 4885 4890	14862
gcg tct ctg aag gcg aac cag acc ctg cgg gca cgt aat gag caa ctg Ala Ser Leu Lys Ala Asn Gln Thr Leu Arg Ala Arg Asn Glu Gln Leu 4895 4900 4905 4910	14910
gca gcc gcc atg gag gcg tcc agc gag ccg att gcg att gtg ggg atg Ala Ala Ala Met Glu Ala Ser Ser Glu Pro Ile Ala Ile Val Gly Met 4915 4920 4925	14958
gcg tgt cgt ttt ccg ggt ggg gtg tgt tcg ccg gag gag ttg tgg gag Ala Cys Arg Phe Pro Gly Gly Val Cys Ser Pro Glu Glu Leu Trp Glu 4930 4935 4940	15006
ctg gtt gcg tcg ggt ggg gat gcg att ggt gaa ttt ccg gcc ggt ccg Leu Val Ala Ser Gly Gly Asp Ala Ile Gly Glu Phe Pro Ala Gly Arg 4945 4950 4955	15054
ggg tgg gat ctg gag ggg ttg ttt gat tcg gac cct gac ccg tcg ggg Gly Trp Asp Leu Glu Gly Leu Phe Asp Ser Asp Pro Asp Arg Ser Gly 4960 4965 4970	15102
acg tcg tac gcg ccg tat ggc ggg ttt ttg tat gag gcg ggg gag ttc Thr Ser Tyr Ala Arg Tyr Gly Gly Phe Leu Tyr Glu Ala Gly Glu Phe 4975 4980 4985 4990	15150
gat gcg gac ttc ttc ggg atc agt ccg cgt gag gcg ttg gcg atg gat Asp Ala Asp Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp 4995 5000 5005	15198
ccg cag cag ccg ttg ttg ctg gag acg tcg tgg gag gcg ttc gag ccg Pro Gln Gln Arg Leu Leu Leu Glu Thr Ser Trp Glu Ala Phe Glu Arg 5010 5015 5020	15246
gcg ggt atc gat ccg ctg tcg atg cgt ggc tcc cgt acg ggt gtc ttc Ala Gly Ile Asp Pro Leu Ser Met Arg Gly Ser Arg Thr Gly Val Phe 5025 5030 5035	15294
gcc ggg gtg atg tac cac gac tac gga tcc cgc ctg ggt acc atc ccc Ala Gly Val Met Tyr His Asp Tyr Gly Ser Arg Leu Gly Thr Ile Pro 5040 5045 5050	15342
gag gga ttc gag ggc tac atc ggc aac ggt agc ggc ggc gcc gtc gcg Glu Gly Phe Glu Gly Tyr Ile Gly Asn Gly Ser Gly Gly Ala Val Ala 5055 5060 5065 5070	15390
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gtg gac acg gca tgt tcg tcg tcg ttg gtg gcg ctg cat ctg gcg tgc Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys 5090 5095 5100	15486
cag tcg ctg ccg tcg ggt gag tgc acg ctc gcg ctg gcc ggc ggt gtg Gln Ser Leu Arg Ser Gly Glu Cys Thr Leu Ala Leu Ala Gly Gly Val 5105 5110 5115	15534

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Thr Val Met Ser Thr Pro His Leu Phe Val Glu Phe Ser Arg Gln Arg	
5120 5125 5130	
gga ctg tcg gtg gac ggc cgc tgc aag tcc ttc gcg ggt gga gcc gac	15630
Gly Leu Ser Val Asp Gly Arg Cys Lys Ser Phe Ala Gly Gly Ala Asp	
5135 5140 5145 5150	
ggc acc ggc atg ggc gag ggc gtc ggg atg ctg ttg gtg gag cgg ttg	15678
Gly Thr Gly Met Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu	
5155 5160 5165	
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Ser Asp Ala Val Arg Leu Gly His Arg Val Leu Ala Val Leu Arg Gly	
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agt gcg gtc aat cag gac ggt gcg tcg aat ggg ttg acg gcg ccg aat	15774
Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn	
5185 5190 5195	
ggt ccg gct cag gag cgg gtg atc cgg cag gcg ttg gcg aac gcg ggg	15822
Gly Pro Ala Gln Glu Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly	
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Leu Ser Val Ala Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr	
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Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly	
5235 5240 5245	
cag cgg gcc ggt aac agg ccg ctg tgg ctg gga tcg gtg aag tcg aac	15966
Gln Arg Ala Gly Asn Arg Pro Leu Trp Leu Gly Ser Val Lys Ser Asn	
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Ile Gly His Ala Gln Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met	
5265 5270 5275	
gtg atg gcg ttg cgg gag ggg gtg ttg ccg cgg acg ttg cat gtg gat	16062
Val Met Ala Leu Arg Glu Gly Val Leu Pro Arg Thr Leu His Val Asp	
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Glu Pro Ser Pro Gln Val Asp Trp Ser Ala Gly Ala Val Arg Leu Leu	
5295 5300 5305 5310	
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Thr Glu Ala Val Pro Trp Pro Gly Asp Ala Ala Gly Arg Leu Arg Arg	
5315 5320 5325	
gcg gga gtg tcg tcg ttc ggg gtc agt ggc acg aat gcg cat gtg att	16206
Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile	
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Leu Glu Glu Ala Pro Ala Ala Gly Gly Cys Val Ala Gly Gly Gly Val	
5345 5350 5355	

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ctg gcg ccg tgg gtg gac tgg tct gtg gtg gac atc ctg cgc ccg gac Leu Ala Pro Trp Val Asp Trp Ser Val Val Asp Ile Leu Arg Arg Asp 5520 5525 5530	16782
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gaa ccc gac gcg gtc ctt ggc cat tcc cag ggc gag atc gcg gcc gcg Glu Pro Asp Ala Val Leu Gly His Ser Gln Gly Glu Ile Ala Ala Ala 5570 5575 5580	16926
cat gtg tgt ggg gcg ctg agc ctg aag gac gcg gcg aag act gtt gcg His Val Cys Gly Ala Leu Ser Leu Lys Asp Ala Ala Lys Thr Val Ala 5585 5590 5595	16974

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Leu Arg Ser Arg Ala Leu Ala Val Arg Gly Arg Gly Gly Met Ala	
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Ser Val Pro Leu Pro Ala Gln Glu Val Glu Gln Leu Ile Gly Glu Arg	
5615 5620 5625 5630	
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Trp Ala Gly Arg Leu Trp Val Ala Ala Val Asn Gly Pro Arg Ser Thr	
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Ala Val Ser Gly Asp Ala Glu Ala Val Asp Glu Val Leu Ala Tyr Cys	
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Ala Gly Thr Gly Val Arg Ala Arg Arg Ile Pro Val Asp Tyr Ala Ser	
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His Cys Pro His Val Gln Pro Leu Arg Glu Glu Leu Leu Glu Leu Leu	
5680 5685 5690	
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Gly Asp Ile Ser Pro Gln Pro Ser Gly Val Pro Phe Phe Ser Thr Val	
5695 5700 5705 5710	
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Glu Gly Thr Trp Leu Asp Thr Thr Thr Leu Asp Ala Ala Tyr Trp Tyr	
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Arg Asn Leu His Gln Pro Val Arg Phe Ser Asp Ala Val Gln Ala Leu	
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Ala Asp Asp Gly His Arg Val Phe Val Glu Val Ser Pro His Pro Thr	
5745 5750 5755	
ctc gtc ccc gcc atc gaa gac acc acc gaa gac acc gcc gaa gac gtc	17502
Leu Val Pro Ala Ile Glu Asp Thr Thr Glu Asp Thr Ala Glu Asp Val	
5760 5765 5770	
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Thr Ala Ile Gly Ser Leu Arg Arg Gly Asp Asn Asp Thr Arg Arg Phe	
5775 5780 5785 5790	
ctc acc gcc ctc gcc cac acc cac acc acc ggc atc ggc aca ccc acc	17598
Leu Thr Ala Leu Ala His Thr His Thr Thr Gly Ile Gly Thr Pro Thr	
5795 5800 5805	
acc tgg cac cac cac tac acc cac cac cac acc cac ccc cac aac cac	17646
Thr Trp His His His Tyr Thr His His His Thr His Pro His Asn His	
5810 5815 5820	
cac ctc gac ctc ccc act tat ccc ttc caa cgc cag cac tac tgg ctc	17694
His Leu Asp Leu Pro Thr Tyr Pro Phe Gln Arg Gln His Tyr Trp Leu	
5825 5830 5835	

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5840			5845			5850										
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5855			5860			5865			5870							
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5875			5880			5885			5885							
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5890			5895			5900										
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5905			5910			5915										
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5920			5925			5930										
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5935			5940			5945			5950							
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5955			5960			5965										
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5970			5975			5980										
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5985			5990			5995										
ccg Pro	ccg Pro	cgg Arg	ggt Gly	gcg Ala	gtg Val	gcg Ala	gtg Val	gat Asp	gtc Val	gat Asp	ggt Gly	gtc Val	cgt Arg	gac Asp	cgt Arg	18222
6000			6005			6010										
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6015			6020			6025			6030							
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6035			6040			6045										
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6050			6055			6060										
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6065			6070			6075										

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tcg gcc ggg cag ggc aac tac gcc gcg gcc aat gcc gct ctg gac gcg Ser Ala Gly Gln Gly Asn Tyr Ala Ala Ala Asn Ala Ala Leu Asp Ala 6515 6520 6525	19758
ctg gcg tac ccg ccg ccg gcg gcg ggt ctg ccg ggg gtg tcg ctg gcg Leu Ala Tyr Arg Arg Arg Ala Ala Gly Leu Pro Gly Val Ser Leu Ala 6530 6535 6540	19806
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Thr Asp His Arg Arg Ile Ile Arg Ser Gly Leu His Pro Met Ser Thr	
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Pro Asp Ala Leu Ala Leu Phe Asp Ala Ala Leu Ala Leu Asp Arg Pro	
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Val Leu Leu Pro Ala Asp Leu Arg Pro Ala Pro Pro Leu Pro Pro Leu	
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Leu Gln Asp Leu Leu Pro Ala Thr Arg Arg Arg Thr Thr Arg Thr Thr	
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Thr Thr Gly Gly Ala Asp Asn Gly Ala Gln Leu His Ala Arg Leu Ala	
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Gly Gln Thr His Glu Gln Gln His Thr Thr Leu Leu Ala Leu Val Arg	
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Ser His Ile Ala Thr Val Leu Gly His Thr Thr Pro Asp Thr Ile Pro	
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Pro Asp Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val	
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Glu Leu Arg Asn Arg Leu Ser Arg Thr Thr Gly Leu Arg Leu Pro Thr	
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His Thr Gln Leu Leu Gly Ser Asp Ser Thr Ala Ser Ile Pro Ala Pro	
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Arg Ala Ala Ala Val Pro Ala Asp Gln Asp Glu Pro Val Ala Ile Ile	
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Gly Met Ala Cys Arg Tyr Pro Gly Gly Val Thr Ser Ala Glu Glu Leu	
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Trp Glu Leu Leu Ala Ser Gly Arg Asp Thr Val Gly Glu Phe Pro Thr	
6770 6775 6780	
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Asp Arg Gly Trp Asp Leu Glu Ala Leu Phe Asp Pro Glu Pro Gly Arg	
6785 6790 6795	

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ctg gcc tgt cag gcg ttg cgt gcg ggt gag tgc tcg atg gcg ctt gcc Leu Ala Cys Gln Ala Leu Arg Ala Gly Glu Cys Ser Met Ala Leu Ala 6930 6935 6940	21006
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acc Thr 7295	ggg Gly 7295	acc Thr 7295	ggg Gly 7300	gag Glu 7300	gcc Ala 7300	gca Ala 7305	gga Gly 7305	aag Lys 7305	acc Thr 7305	gca Ala 7310	ttc Phe 7310	atc Ile 7310	tgc Cys 7310	tcc Ser 7310	gga Gly 7310	22110
cag Gln 7315	ggc Gly 7315	acc Thr 7315	caa Gln 7315	cgc Arg 7315	ccc Pro 7320	ggc Gly 7320	atg Met 7320	gcc Ala 7325	cac His 7325	ggc Gly 7325	ctc Leu 7325	tac Tyr 7325	cac His 7325	acc Thr 7325	cac His 7325	22158
ccc Pro 7330	gtc Val 7330	ttc Phe 7330	gcc Ala 7335	gcc Ala 7335	gca Ala 7340	ctc Leu 7340	aac Asn 7340	gac Asp 7340	atc Ile 7340	tgc Cys 7340	acc Thr 7340	cac His 7340	ctc Leu 7340	gac Asp 7340	ccc Pro 7340	22206
cac His 7345	ctc Leu 7345	gac Asp 7345	cac His 7350	ccc Pro 7350	ctc Leu 7350	ctc Leu 7350	ccc Pro 7350	ctc Leu 7355	ctc Leu 7355	acc Thr 7355	cag Gln 7355	gac Asp 7355	ccc Pro 7355	aac Asn 7355	acc Thr 7355	22254
cag Gln 7360	gac Asp 7360	acc Thr 7360	acc Thr 7365	acc Thr 7365	ctc Leu 7365	gaa Glu 7370	gaa Glu 7370	gcg Ala 7370	gcc Ala 7370	gca Ala 7370	ctg Leu 7370	ctc Leu 7370	cag Gln 7370	cag Gln 7370	acc Thr 7370	22302
ccg Pro 7375	tac Tyr 7375	gcc Ala 7380	cag Gln 7380	ccc Pro 7380	gcc Ala 7380	ctc Leu 7385	ttc Phe 7385	gcc Ala 7385	ttc Phe 7385	cag Gln 7385	gtc Val 7385	gcc Ala 7390	ctc Leu 7390	cac His 7390	cgc Arg 7390	22350
ctc Leu 7395	ctc Leu 7395	acc Thr 7395	gac Asp 7395	ggc Gly 7395	tac Tyr 7400	cac His 7400	atc Ile 7400	acc Thr 7400	ccc Pro 7405	cac His 7405	tac Tyr 7405	tac Tyr 7405	gcc Ala 7405	gga Gly 7405	cac His 7405	22398
tcc Ser 7410	ctc Leu 7410	ggc Gly 7410	gaa Glu 7415	atc Ile 7415	acc Thr 7415	gcc Ala 7415	gcc Ala 7415	cac His 7415	ctc Leu 7415	gcc Ala 7420	ggc Gly 7420	atc Ile 7420	ctc Leu 7420	acc Thr 7420	ctc Leu 7420	22446
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aac Asn 7475	acc Thr 7475	ccc Pro 7475	acc Thr 7475	tcc Ser 7475	ctc Leu 7475	gtc Val 7480	atc Ile 7480	agc Ser 7480	ggc Gly 7480	acc Thr 7480	ccc Pro 7485	cac His 7485	acc Thr 7485	gtc Val 7485	caa Gln 7485	22638
cac His 7490	atc Ile 7490	acc Thr 7490	acc Thr 7490	ctc Leu 7490	tgc Cys 7495	caa Gln 7495	caa Gln 7495	caa Gln 7495	ggc Gly 7495	atc Ile 7500	aaa Lys 7500	acc Thr 7500	aaa Lys 7500	acc Thr 7500	ctc Leu 7500	22686
ccc Pro 7505	acc Thr 7505	aac Asn 7505	cac His 7510	gcc Ala 7510	ttc Phe 7510	cac His 7510	tcc Ser 7510	ccc Pro 7510	cac His 7515	acc Thr 7515	aac Asn 7515	ccc Pro 7515	atc Ile 7515	ctc Leu 7515	aac Asn 7515	22734

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ccc ctc atc acc gcc aac acc cca ccc gac caa ctc ctc acc ccc cac Pro Leu Ile Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His 7535 7540 7545 7550	22830
tac tgg acc caa caa gcc cgc aac acc gtc gac ata gcc acc acc acc Tyr Trp Thr Gln Gln Ala Arg Asn Thr Val Asp Ile Ala Thr Thr Thr 7555 7560 7565	22878
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cgc tac ggc gac gac atc ctc gtc gag gca cgt ctt ccc gaa gaa gtg Arg Tyr Gly Asp Asp Ile Leu Val Glu Ala Arg Leu Pro Glu Glu Val 7855 7860 7865 7870	23790
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Arg	Cys	Pro	Asp	Ala	Gly	Ala	Asp	Gly	Gly	Gly	Gly	Gly	Gly	Val	Gly	
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Glu	Val	Val	Gly	Gly	Val	Leu	Gly	Val	Val	Gln	Gly	Trp	Leu	Gly	Leu	
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Glu	Arg	Phe	Ala	Gly	Ser	Arg	Leu	Val	Val	Val	Thr	Arg	Gly	Ala	Val	
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Val	Ala	Gly	Pro	Glu	Asp	Gly	Pro	Val	Asp	Val	Val	Gly	Ala	Ala	Val	
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Trp	Gly	Leu	Val	Arg	Ser	Ala	Gln	Ala	Glu	His	Pro	Asp	Arg	Phe	Val	
8080			8085			8090										
ctc	ctc	gac	ctg	gac	acc	gac	ctc	gac	agc	ggc	gct	gac	gcc	gat	gcc	24510
Leu	Leu	Asp	Leu	Asp	Thr	Asp	Leu	Asp	Ser	Gly	Ala	Asp	Ala	Asp	Ala	
8095			8100			8105							8110			
ggc	aac	gag	gcc	ggt	atg	ggg	tct	ggt	ctg	gat	ggt	ggg	cgt	gtg	gct	24558
Gly	Asn	Glu	Ala	Gly	Met	Gly	Ser	Gly	Leu	Asp	Gly	Gly	Arg	Val	Ala	
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Ala	Val	Val	Ala	Cys	Gly	Glu	Pro	Gln	Leu	Ala	Val	Arg	Gly	Glu	Arg	
8130			8135			8140										
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Val	Leu	Ala	Ala	Arg	Leu	Thr	Arg	Leu	Glu	Ser	Pro	Val	Asp	Val	Ser	
8145			8150			8155										
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Gly	Arg	Glu	Val	Leu	Pro	Trp	Leu	Ser	Gly	Gly	Ser	Val	Leu	Val	Thr	
8160			8165			8170										
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Gly	Gly	Thr	Gly	Val	Leu	Gly	Ala	Ala	Val	Ala	Arg	His	Leu	Ala	Gly	
8175			8180			8185							8190			
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Val	Cys	Gly	Val	Arg	Asp	Leu	Leu	Leu	Val	Ser	Arg	Arg	Gly	Pro	Asp	
8195			8200			8205										
gct	ccg	ggt	gcg	gag	ggt	ttg	cgg	gcg	gag	ctg	gcc	gcg	ttg	ggg	gcg	24846
Ala	Pro	Gly	Ala	Glu	Gly	Leu	Arg	Ala	Glu	Leu	Ala	Ala	Leu	Gly	Ala	
8210			8215			8220										
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Glu	Val	Arg	Ile	Val	Ala	Cys	Asp	Val								

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cat gcg gct ggt gtg ctg gac gat gcg acg atc gcc tct ctc acg ccc His Ala Ala Gly Val Leu Asp Asp Ala Thr Ile Ala Ser Leu Thr Pro 8255 8260 8265 8270	24990
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ctg gat gag ctg acg cgg ggt atg gag ctg tcg gcg ttc gtg ctg ttc Leu Asp Glu Leu Thr Arg Gly Met Glu Leu Ser Ala Phe Val Leu Phe 8290 8295 8300	25086
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acc acc ctc ctc gcc ctg gtc cgc tcc cac atc gcc acc gtc ctc ggc Thr Thr Leu Leu Ala Leu Val Arg Ser His Ile Ala Thr Val Leu Gly 8450 8455 8460	25566
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tac gcc gcg cgt ctc cac cat gtc ccc gag ggt ttc gaa ggc ctc atc Tyr Ala Ala Arg Leu His His Val Pro Glu Gly Phe Glu Gly Leu Ile 8675 8680 8685	26238
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 50 55 60
 Ala Pro Tyr Val Asp Trp Ser Val Glu Gln Val Leu Arg Asp Ser Pro
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 Asp Ala Pro Gly Leu Asp Arg Val Asp Val Val Gln Pro Thr Leu Phe
 85 90 95
 Ala Val Met Ile Ser Leu Ala Ala Leu Trp Arg Ser Gln Gly Val Glu
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 Pro Cys Ala Val Leu Gly His Ser Leu Gly Glu Ile Ala Ala Ala His
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 Asp Leu Thr Ala Ala Gln Val Arg Thr Arg Met Ile Pro Val Asp Val
 210 215 220
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Ile	Gly	Pro	Phe	Pro	Thr	Asp	Arg	Gly	Trp	Pro	Thr	Glu	Gln	Arg	His		
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Phe	Leu	His	Asp	Ala	Ala	His	Phe	Asp	Ala	Gly	Phe	Phe	Gly	Ile	Ser		
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	690					695					700				
Asp	Gly	Arg	Cys	Lys	Ala	Tyr	Ser	Ala	Ala	Ala	Asp	Gly	Thr	Gly	Trp
	705				710					715					720
Gly	Glu	Gly	Val	Gly	Met	Leu	Leu	Val	Glu	Arg	Leu	Ser	Asp	Ala	Val
				725					730					735	
Arg	Leu	Gly	His	Arg	Val	Leu	Ala	Val	Val	Arg	Gly	Ser	Ala	Val	Asn
			740					745					750		
Gln	Asp	Gly	Ala	Ser	Asn	Gly	Leu	Thr	Ala	Pro	Asn	Gly	Pro	Ala	Gln
		755					760					765			
Glu	Arg	Val	Ile	Arg	Gln	Ala	Leu	Ala	Asn	Ala	Gly	Leu	Ser	Val	Ala
	770					775					780				
Asp	Val	Asp	Val	Val	Glu	Gly	His	Gly	Thr	Gly	Thr	Thr	Leu	Gly	Asp
	785				790				795						800
Pro	Ile	Glu	Ala	Gln	Ala	Leu	Leu	Ala	Thr	Tyr	Gly	Gln	Arg	Ala	Gly
				805					810					815	
Asp	Arg	Pro	Leu	Trp	Leu	Gly	Ser	Leu	Lys	Ser	Asn	Ile	Gly	His	Thr
			820					825					830		
Met	Ala	Ala	Ala	Gly	Val	Gly	Gly	Val	Ile	Lys	Met	Val	Met	Ala	Leu
		835					840					845			
Arg	Glu	Gly	Val	Leu	Pro	Arg	Thr	Leu	His	Val	Asp	Lys	Pro	Ser	Pro
	850					855					860				
Gln	Val	Asp	Trp	Ser	Ala	Gly	Ala	Val	Arg	Leu	Leu	Thr	Glu	Ala	Val
	865				870				875						880
Pro	Trp	Pro	Gly	Asp	Ala	Ala	Gly	Arg	Leu	Arg	Arg	Ala	Gly	Val	Ser
				885					890					895	
Ser	Phe	Gly	Ile	Gly	Gly	Thr	Asn	Ala	His	Val	Ile	Leu	Glu	Glu	Ala
			900					905					910		

Pro Ala Ala Gly Gly Cys Val Ala Gly Gly Gly Val Leu Glu Gly Ala
915 920 925

Pro Gly Leu Ala Ile Ser Val Ala Glu Ser Val Ala Ala Pro Val Ala
930 935 940

Val Ser Ala Pro Val Ala Glu Ser Val Pro Val Pro Val Pro Val Pro
945 950 955 960

Val Pro Val Pro Val Ser Ala Arg Ser Glu Ala Gly Leu Arg Ala Gln
965 970 975

Ala Glu Ala Leu Arg Gln Tyr Val Ala Val Arg Pro Asp Val Ser Leu
980 985 990

Ala Asp Val Gly Ala Gly Leu Ala Cys Gly Arg Ala Val Leu Glu His
995 1000 1005

Arg Ala Val Val Leu Ala Ala Asp Arg Glu Glu Leu Val Gln Gly Leu
1010 1015 1020

Gly Ala Leu Ala Ala Gly Glu Pro Asp Arg Arg Val Thr Thr Gly His
1025 1030 1035 1040

Ala Pro Gly Gly Asp Arg Gly Gly Val Val Phe Val Phe Pro Gly Gln
1045 1050 1055

Gly Gly Gln Trp Ala Gly Met Gly Val Arg Leu Leu Ala Ser Ser Pro
1060 1065 1070

Val Phe Ala Arg Arg Met Gln Ala Cys Glu Glu Ala Leu Ala Pro Trp
1075 1080 1085

Val Asp Trp Ser Val Val Asp Ile Leu Arg Arg Asp Ala Gly Asp Ala
1090 1095 1100

Val Trp Glu Arg Ala Asp Val Val Gln Pro Val Leu Phe Ser Val Met
1105 1110 1115 1120

Val Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Ile Glu Pro Asp Ala
1125 1130 1135

Val Leu Gly His Ser Gln Gly Glu Ile Ala Ala Ala His Val Cys Gly
1140 1145 1150

Ala Leu Ser Leu Lys Asp Ala Ala Lys Thr Val Ala Leu Arg Ser Arg
1155 1160 1165

Ala Leu Ala Ala Val Arg Gly Arg Gly Gly Met Ala Ser Val Pro Leu
1170 1175 1180

Pro Ala Gln Glu Val Glu Gln Leu Ile Gly Glu Arg Trp Ala Gly Arg
1185 1190 1195 1200

Leu Trp Val Ala Ala Val Asn Gly Pro Arg Ser Thr Ala Val Ser Gly
1205 1210 1215

Asp Ala Glu Ala Val Asp Glu Val Leu Ala Tyr Cys Ala Gly Thr Gly
1220 1225 1230

Val Arg Ala	Arg Arg Ile	Pro Val Asp	Tyr Ala Ser	His Cys Pro	His
1235		1240		1245	
Val Gln Pro	Leu Arg Glu	Glu Glu Leu	Leu Leu Glu	Leu Leu Gly	Asp Ile Ser
1250		1255		1260	
Pro Gln Pro	Ser Gly Val	Pro Phe Phe	Ser Thr Val	Glu Gly Thr	Trp
1265		1270		1275	1280
Leu Asp Thr	Thr Thr Leu	Asp Ala Ala	Tyr Trp Tyr	Arg Asn Leu	His
	1285		1290		1295
Gln Pro Val	Arg Phe Ser	Asp Ala Val	Gln Ala Leu	Ala Asp Asp	Gly
	1300		1305		1310
His Arg Val	Phe Val Glu	Val Ser Pro	His Pro Thr	Leu Val Pro	Ala
	1315		1320		1325
Ile Glu Asp	Thr Thr Glu	Asp Thr Ala	Glu Asp Val	Thr Ala Ile	Gly
	1330		1335		1340
Ser Leu Arg	Arg Gly Asp	Asn Asp Thr	Arg Arg Phe	Leu Thr Ala	Leu
1345		1350		1355	1360
Ala His Thr	His Thr Thr	Gly Ile Gly	Thr Pro Thr	Thr Trp His	His
	1365		1370		1375
His Tyr Thr	His His His	Thr His Pro	His Pro His	Thr His Leu	Asp
	1380		1385		1390
Leu Pro Thr	Tyr Pro Phe	Gln His Gln	His Tyr Trp	Leu Glu Ser	Ser
	1395		1400		1405
Gln Pro Gly	Ala Gly Ser	Gly Ser Gly	Ala Gly Ala	Gly Ser Gly	Ala
	1410		1415		1420
Gly Ser Gly	Arg Ala Gly	Thr Ala Gly	Gly Thr Ala	Glu Val Glu	Ser
1425		1430		1435	1440
Arg Phe Trp	Asp Ala Val	Ala Arg Gln	Asp Leu Glu	Thr Val Ala	Thr
	1445		1450		1455
Thr Leu Ala	Val Pro Pro	Ser Ala Gly	Leu Asp Thr	Val Val Pro	Ala
	1460		1465		1470
Leu Ser Ala	Trp His Arg	His Gln His	Asp Gln Ala	Arg Ile Asn	Thr
	1475		1480		1485
Trp Thr Tyr	Gln Glu Thr	Trp Lys Pro	Leu Thr Leu	Pro Thr Thr	His
	1490		1495		1500
Gln Pro His	Gln Thr Trp	Leu Ile Ala	Ile Pro Glu	Thr Gln Thr	His
1505		1510		1515	1520
His Pro His	Ile Thr Asn	Ile Leu Thr	Asn Leu His	His His Gly	Ile
	1525		1530		1535
Thr Pro Ile	Pro Leu Thr	Leu Asn His	Thr His Thr	Asn Pro Gln	His
	1540		1545		1550

Leu His His Thr Leu His His Thr Arg Gln Gln Ala Gln Asn His Thr
 1555 1560 1565
 Thr Gly Ala Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu Asp Glu Thr
 1570 1575 1580
 Pro His Pro His His Pro His Thr Pro Thr Gly Thr Leu Leu Asn Leu
 1585 1590 1595 1600
 Thr Leu Thr Gln Thr His Thr Gln Thr His Pro Pro Thr Pro Leu Trp
 1605 1610 1615
 Tyr Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp Pro Leu Thr
 1620 1625 1630
 His Pro Thr Gln Ala Gln Thr Trp Gly Leu Ala Arg Thr Thr Leu Leu
 1635 1640 1645
 Glu His Pro Thr His Thr Ala Gly Ile Ile Asp Leu Pro Thr Thr Pro
 1650 1655 1660
 Thr Pro His Thr Leu Gln His Leu Thr Gln Thr Leu Thr Gln Pro His
 1665 1670 1675 1680
 His Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His Thr Arg Arg
 1685 1690 1695
 Leu Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro Thr Pro Thr
 1700 1705 1710
 Pro His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala Leu Ala Thr
 1715 1720 1725
 His Leu Thr His His Leu Thr Thr His Gln Pro Thr Gln His Leu Leu
 1730 1735 1740
 Leu Thr Ser Arg Thr Gly Pro His Thr Pro His Ala Gln His Leu Thr
 1745 1750 1755 1760
 Thr Gln Leu Gln Gln Lys Gly Ile His Leu Thr Ile Thr Thr Cys Asp
 1765 1770 1775
 Thr Ser Asn Pro Asp Gln Leu Gln Gln Leu Leu Asn Thr Ile Pro Pro
 1780 1785 1790
 Gln His Pro Leu Thr Thr Val Ile His Thr Ala Gly Ile Leu Asp Asp
 1795 1800 1805
 Ala Thr Leu Thr Asn Leu Thr Pro Thr Gln Leu Asn Asn Val Leu Arg
 1810 1815 1820
 Ala Lys Ala His Ser Ala His Leu Leu His Gln Leu Thr Gln His Thr
 1825 1830 1835 1840
 Pro Leu Thr Ala Phe Val Leu Tyr Ser Ser Ala Ala Ala Thr Phe Gly
 1845 1850 1855
 Ala Pro Gly Gln Ala Asn Tyr Ala Ala Ala Asn Ala Tyr Leu Asp Ala
 1860 1865 1870

Leu Ala His His Arg His Thr His His Leu Pro Ala Thr Ser Ile Ala
1875 1880 1885

Trp Gly Thr Trp Gln Gly Asn Gly Leu Ala Asp Ser Asp Lys Ala Arg
1890 1895 1900

Ala Tyr Leu Asp Arg Arg Gly Phe Arg Pro Met Ser Pro Glu Leu Ala
1905 1910 1915 1920

Thr Ala Ala Val Thr Gln Ala Ile Ala Asp Thr Glu Arg Pro Tyr Val
1925 1930 1935

Val Ile Ala Asp Ile Asp Trp Ser Lys Ile Glu His Thr Ser Gln Thr
1940 1945 1950

Ser Asp Leu Val Ser Ala Ala Arg Glu Arg Glu Pro Ala Val Gln Arg
1955 1960 1965

Pro Thr Pro Pro Ala Glu Leu His Lys Thr Leu Ala His Gln Thr Ser
1970 1975 1980

Ala Asp Gln Arg Ala Ala Leu Leu Glu Leu Val Arg Asp His Val Ala
1985 1990 1995 2000

Ala Val Leu Arg His Ala Asp Pro Lys Ala Ile Ala Pro Asp Gln Ser
2005 2010 2015

Phe Arg Ala Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Phe Arg Asn
2020 2025 2030

Leu Leu Ile Lys Ala Thr Gly Leu Arg Leu Pro Val Ser Leu Val Phe
2035 2040 2045

Asp His Pro Thr Pro Ala Lys Leu Ala Val His Leu Gln Asn Gln Leu
2050 2055 2060

Arg Gly Thr Ala Ala Glu Ser Ala Pro Ser Ala Ala Val Thr Ala
2065 2070 2075 2080

Glu Ala Ser Val Thr Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg
2085 2090 2095

Phe Pro Gly Gly Val Thr Ser Ala Asp Asp Phe Trp Asp Leu Ile Ser
2100 2105 2110

Ser Glu Gln Asp Ala Ile Gly Gly Phe Pro Thr Asp Arg Gly Trp Asp
2115 2120 2125

Leu Asp Thr Leu Tyr Asp Pro Asp Pro Asp His Pro Gly Thr Cys Tyr
2130 2135 2140

Thr Arg Asn Gly Gly Phe Leu Tyr Asp Ala Gly His Phe Asp Ala Glu
2145 2150 2155 2160

Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln
2165 2170 2175

Arg Leu Leu Leu Glu Thr Ala Trp Glu Thr Ile Glu His Ala Gly Ile
2180 2185 2190

Asn	Pro	His	Thr	Leu	His	Gly	Thr	Pro	Thr	Gly	Val	Phe	Thr	Gly	Thr	2195	2200	2205
Asn	Gly	Gln	Asp	Tyr	Ala	Leu	Arg	Val	His	Asn	Ala	Gly	Gln	Ser	Thr	2210	2215	2220
Asp	Gly	Phe	Ala	Leu	Thr	Gly	Thr	Ala	Gly	Ser	Val	Ile	Ser	Gly	Arg	2225	2230	2235
Ile	Ser	Tyr	Thr	Phe	Gly	Phe	Glu	Gly	Pro	Ala	Val	Ser	Val	Asp	Thr	2245	2250	2255
Ala	Cys	Ser	Ser	Ser	Leu	Val	Ala	Leu	His	Leu	Ala	Cys	Gln	Ala	Leu	2260	2265	2270
Arg	Ala	Gly	Glu	Cys	Ser	Met	Ala	Leu	Ala	Gly	Gly	Val	Thr	Val	Met	2275	2280	2285
Ser	Ser	Pro	Gly	Ala	Phe	Val	Glu	Phe	Ser	Arg	Gln	Arg	Gly	Leu	Ala	2290	2295	2300
Ala	Asp	Gly	His	Cys	Lys	Ala	Phe	Ser	Ala	Ala	Ala	Asp	Gly	Thr	Gly	2305	2310	2315
Trp	Gly	Glu	Gly	Val	Gly	Met	Leu	Leu	Val	Glu	Arg	Leu	Ser	Asp	Ala	2325	2330	2335
His	Arg	Asn	Gly	His	Arg	Val	Leu	Ala	Val	Val	Arg	Gly	Ser	Ala	Val	2340	2345	2350
Asn	Gln	Asp	Gly	Ala	Ser	Asn	Gly	Leu	Thr	Ala	Pro	Asn	Gly	Pro	Ser	2355	2360	2365
Gln	Gln	Arg	Val	Ile	Arg	Gln	Ala	Leu	Ala	Asn	Ala	Gly	Leu	Ser	Ala	2370	2375	2380
Gly	Asp	Val	Asp	Ala	Val	Glu	Ala	His	Gly	Thr	Gly	Thr	Thr	Leu	Gly	2385	2390	2395
Asp	Pro	Ile	Glu	Ala	Gln	Ala	Leu	Leu	Ala	Thr	Tyr	Gly	Gln	Asp	Arg	2405	2410	2415
Ala	Gly	Glu	Gly	Pro	Leu	Trp	Leu	Gly	Ser	Val	Lys	Ser	Asn	Val	Gly	2420	2425	2430
His	Thr	Gln	Ala	Ala	Ala	Gly	Val	Ala	Gly	Val	Ile	Lys	Met	Val	Met	2435	2440	2445
Ala	Leu	Arg	His	Gly	Leu	Leu	Pro	Arg	Thr	Leu	His	Val	Asp	Glu	Pro	2450	2455	2460
Ser	Pro	His	Val	Asp	Trp	Ser	Ala	Gly	Ala	Val	Gln	Leu	Leu	Thr	Glu	2465	2470	2475
Thr	Val	Pro	Trp	Pro	Gly	Gly	Glu	Gly	Arg	Leu	Arg	Arg	Ala	Gly	Val	2485	2490	2495
Ser	Ser	Phe	Gly	Val	Ser	Gly	Thr	Asn	Ala	His	Val	Ile	Leu	Glu	Glu	2500	2505	2510

Ala Pro Ala Asp Asp Val Pro Gly Gly Pro Pro Ala Gly Glu Gly Asp
 2515 2520 2525
 Ala Gly Ser Asp Asp Glu Ala Ala Ala Gly Ser Pro Gly Val Trp Pro
 2530 2535 2540
 Trp Leu Val Ser Ala Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln
 2545 2550 2555 2560
 Ala Leu His Ala His Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp
 2565 2570 2575
 Val Gly Tyr Thr Leu Ala His Ala Arg Ala Val Phe Asp His Arg Ala
 2580 2585 2590
 Thr Leu Ile Ala Ala Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala
 2595 2600 2605
 Leu Ala Ala Gly Glu Pro His Pro Ala Val Ile His Ser Ser Ala Pro
 2610 2615 2620
 Gly Gly Thr Gly Thr Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys
 2625 2630 2635 2640
 Ser Gly Gln Gly Thr Gln Arg Pro Gly Met Ala His Gly Leu Tyr His
 2645 2650 2655
 Thr His Pro Val Phe Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu
 2660 2665 2670
 Asp Pro His Leu Asp His Pro Leu Leu Pro Leu Leu Thr Gln Asn Asp
 2675 2680 2685
 Asn Asp Asn Glu Asp Ala Ala Ala Leu Leu Gln Gln Thr Arg Tyr Ala
 2690 2695 2700
 Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr
 2705 2710 2715 2720
 Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly
 2725 2730 2735
 Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala
 2740 2745 2750
 Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro
 2755 2760 2765
 Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His His
 2770 2775 2780
 Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro
 2785 2790 2795 2800
 Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr
 2805 2810 2815
 Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Asn
 2820 2825 2830

004230 98341650

His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His
 2835 2840 2845

Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile
 2850 2855 2860

Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr
 2865 2870 2875 2880

Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr Leu
 2885 2890 2895

His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr
 2900 2905 2910

Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Pro Pro Thr Thr Thr
 2915 2920 2925

Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu Thr
 2930 2935 2940

Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr His
 2945 2950 2955 2960

His Asp Asn Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr
 2965 2970 2975

Pro Phe Gln His His His Tyr Trp Leu Glu Ser Thr Gln Pro Gly Ala
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Gly Asn Val Ser Ala Ala Gly Leu Asp Pro Thr Glu His Pro Leu Leu
 2995 3000 3005

Gly Ala Thr Leu Glu Leu Ala Thr Asp Gly Gly Ala Leu Leu Ala Gly
 3010 3015 3020

Arg Leu Ser Leu Arg Ser His Pro Trp Leu Ala Asp His Ala Val Gly
 3025 3030 3035 3040

Gly Thr Val Leu Leu Ser Gly Ala Thr Phe Leu Glu Leu Ala Leu His
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Ala Gly Thr Tyr Val Gly Cys Asp Arg Val Asp Glu Leu Thr Leu His
 3060 3065 3070

Ala Pro Leu Val Val Pro Val Asp Gly Gly Val Ser Val Gln Val Gly
 3075 3080 3085

Val Ala Ala Ala Asp Gly Glu Gly Arg Arg Leu Val Ser Val Tyr Ala
 3090 3095 3100

Arg Gly Gly Ser Ala Cys Gly Gly Gly Gly Ala Ser Gly Gly Val Trp
 3105 3110 3115 3120

Thr Cys His Ala Ser Gly Val Leu Val Glu Ala Ala Ala Gly Gly Val
 3125 3130 3135

Val Val Asp Gly Leu Ala Gly Val Trp Pro Pro Arg Gly Ala Val Ala
 3140 3145 3150

Val Asp Val	Asp Gly Val	Arg Asp Arg	Leu Ala Gly	Ala Gly Cys Val
3155		3160		3165
Leu Gly Pro	Val Phe Ser	Gly Leu Arg	Ala Val Trp	Arg Asp Gly Gly
3170		3175		3180
Asp Leu Leu	Ala Glu Val	Cys Leu Pro	Glu Glu Ala	Trp Gly Asp Ala
3185		3190		3195 3200
Ala Gly Phe	Gly Leu His	Pro Ala Leu	Leu Asp Gly	Val Val Gln Pro
	3205		3210	3215
Leu Ser Val	Leu Leu Pro	Gly Gly Thr	Gly Phe Gly	Glu Gly Ala Gly
	3220		3225	3230
Phe Gly Glu	Gly Val Arg	Val Pro Ala	Val Trp Gly	Gly Gly Val Ser Leu
	3235		3240	3245
His Arg Ala	Gly Val Thr	Gly Val Arg	Val Arg Val	Ser Ala Val Gly
	3250		3255	3260
Arg Gly Gly	Gly Arg Glu	Ala Val Ser	Val Val Val	Gly Asp Glu Ala
3265		3270		3275 3280
Gly Val Pro	Val Ala Ser	Val Asp Arg	Leu Glu Leu	Arg Pro Val Asp
	3285		3290	3295
Met Gly Gln	Leu Arg Ala	Val Ser Val	Ser Ala Gly	Arg Arg Gly Ser
	3300		3305	3310
Leu Tyr Ala	Val Gln Trp	Ala Glu Val	Gly Pro Val	Pro Val Cys Gly
	3315		3320	3325
Gln Ala Trp	Ala Trp His	Glu Asp Val	Gly Glu Ser	Gly Gly Gly Pro
	3330		3335	3340
Val Pro Gly	Val Val Val	Leu Arg Cys	Pro Asp Ala	Gly Ala Gly Gly
3345		3350		3355 3360
Gly Gly Gly	Gly Gly Gly	Gly Gly Gly	Val Gly Glu	Val Val Gly Gly
	3365		3370	3375
Val Leu Gly	Val Val Gln	Gly Trp Leu	Gly Leu Glu	Arg Phe Ala Gly
	3380		3385	3390
Ser Arg Leu	Val Val Val	Thr Arg Gly	Ala Val Val	Ala Gly Pro Glu
	3395		3400	3405
Asp Gly Pro	Val Asp Val	Val Gly Ala	Ser Val Trp	Gly Leu Val Arg
	3410		3415	3420
Ser Ala Gln	Ala Glu His	Pro Asp Arg	Phe Val Leu	Leu Asp Leu Asp
3425		3430		3435 3440
Thr Asp Thr	Gly Thr Asp	Leu Asp Thr	Gly Ala Gly	Ala Gly Trp Gly
	3445		3450	3455
Val Asp Gly	Gly Arg Val	Ala Ala Val	Val Val Ala	Cys Gly Glu Pro Gln
	3460		3465	3470

Leu Ala Val Arg Gly Glu Arg Leu Leu Ala Ala Arg Leu Lys Arg Leu
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 Glu Ser Ser Gly Asp Val Pro Ala Gln Arg Ser Gly Asp Thr Arg Ala
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 Arg Arg Ser Asp Val Pro Ala Gln Arg Ser Gly Gly Val Pro Ala Arg
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 Arg Ser Val Asp Val Ser Gly Arg Glu Val Leu Pro Trp Leu Ser Gly
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 Gly Ser Val Leu Val Thr Gly Gly Thr Gly Val Leu Gly Ala Ala Val
 3540 3545 3550
 Ala Arg His Leu Ala Gly Val Cys Gly Val Arg Asp Leu Leu Leu Val
 3555 3560 3565
 Ser Arg Arg Gly Pro Asp Ala Pro Gly Ala Glu Gly Leu Arg Ala Glu
 3570 3575 3580
 Leu Ala Ala Leu Gly Ala Glu Val Arg Ile Val Ala Cys Asp Val Gly
 3585 3590 3595 3600
 Glu Arg Arg Glu Val Val Arg Leu Leu Glu Gly Val Pro Ala Gly Cys
 3605 3610 3615
 Pro Leu Thr Gly Val Val His Ala Ala Gly Val Leu Asp Asp Ala Thr
 3620 3625 3630
 Ile Ala Ser Leu Thr Pro Glu Arg Leu Gly Thr Val Phe Ala Ala Lys
 3635 3640 3645
 Val Asp Ala Ala Leu Leu Leu Asp Glu Leu Thr Arg Gly Met Glu Leu
 3650 3655 3660
 Ser Ala Phe Val Leu Phe Ser Ser Ala Ala Gly Ile Leu Gly Ser Ala
 3665 3670 3675 3680
 Gly Gln Gly Asn Tyr Ala Ala Ala Asn Ala Ala Leu Asp Ala Leu Ala
 3685 3690 3695
 Tyr Arg Arg Arg Ala Ala Gly Leu Pro Gly Val Ser Leu Ala Trp Gly
 3700 3705 3710
 Leu Trp Glu Glu Ala Ser Gly Met Thr Gly His Leu Ala Gly Thr Asp
 3715 3720 3725
 His Arg Arg Ile Ile Arg Ser Gly Leu His Pro Met Ser Thr Pro Asp
 3730 3735 3740
 Ala Leu Ala Leu Phe Asp Ala Ala Leu Ala Leu Asp Arg Pro Val Leu
 3745 3750 3755 3760
 Leu Pro Ala Asp Leu Arg Pro Ala Pro Pro Leu Pro Pro Leu Leu Gln
 3765 3770 3775
 Asp Leu Leu Pro Ala Thr Arg Arg Arg Thr Thr Arg Thr Thr Thr Thr
 3780 3785 3790

Gly Gly Ala Asp Asn Gly Ala Gln Leu His Ala Arg Leu Ala Gly Gln
3795 3800 3805

Thr His Glu Gln Gln His Thr Thr Leu Leu Ala Leu Val Arg Ser His
3810 3815 3820

Ile Ala Thr Val Leu Gly His Thr Thr Pro Asp Thr Ile Pro Pro Asp
3825 3830 3835 3840

Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu
3845 3850 3855

Arg Asn Arg Leu Ser Arg Thr Thr Gly Leu Arg Leu Pro Thr Thr Leu
3860 3865 3870

Ala Phe Asp His Pro Asn Pro Thr Thr Leu Thr His His Leu His Thr
3875 3880 3885

Gln Leu Gln Pro Gln Pro Asp Asn Ala Val Ala Pro Val Leu Ala Glu
3890 3895 3900

Leu Asp Lys Leu Glu Ser Ala Leu Ser Ala Leu Asp Lys Thr Asp Ser
3905 3910 3915 3920

Ala Ser Glu Arg Val Thr Leu Arg Leu Lys Ser Leu Met Leu Arg Trp
3925 3930 3935

Asn Ala Pro Gln His Pro Thr Ala Glu Ser Ala Asp Asp Asp Glu Lys
3940 3945 3950

Phe Thr Ser Ala Thr Glu Ala Glu Ile Phe Lys Phe Ile Asp Asn Asp
3955 3960 3965

Leu Gly Leu Ser
3970

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<211> 6239

<212> PRT

<213> Streptomyces avermitilis

<400> 4

Met Gln Leu Ala Asn Glu Ala Lys Leu Leu Glu Tyr Leu Lys Arg Val
1 5 10 15

Thr Ala Asp Leu Asp Arg Thr Arg Arg Arg Leu Tyr Glu Val Val Glu
20 25 30

Arg Glu Gln Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Tyr Pro
35 40 45

Gly Gly Ala Thr Ser Pro Thr Arg Leu Trp His Leu Val Lys Ser Gln
50 55 60

Thr Asp Ala Ile Gly Glu Phe Pro Thr Asp Arg Gly Trp Asn Leu Glu
65 70 75 80

Gln Leu Tyr Asp Pro Asp Pro Asp Arg Ser Gly Thr Ser Tyr Thr Arg
85 90 95

Ser	Gly	Gly	Phe	Leu	Tyr	Asp	Ala	Gly	Asp	Phe	Asp	Ala	Ala	Phe	Phe	
			100					105					110			
Glu	Leu	Ser	Pro	Arg	Glu	Ala	Leu	Ala	Met	Asp	Pro	Gln	Gln	Arg	Leu	
		115					120					125				
Leu	Leu	Glu	Thr	Thr	Trp	Glu	Thr	Phe	Glu	Gln	Gly	Gly	Ile	Asp	Pro	
		130				135					140					
Arg	Ser	Met	Arg	Gly	Ser	Arg	Thr	Gly	Val	Phe	Val	Gly	Ile	Asn	Pro	
145					150					155					160	
Glu	Asp	Tyr	Thr	Thr	Gly	Tyr	Thr	His	Gln	Pro	Ser	Asn	Ala	Val	Glu	
				165					170					175		
Gly	Tyr	Leu	Leu	Thr	Gly	Ser	Ala	Ala	Ser	Ile	Ala	Ser	Gly	Arg	Ile	
			180					185					190			
Ser	Tyr	Asn	Phe	Gly	Leu	Glu	Gly	Pro	Ala	Ile	Thr	Ile	Asp	Thr	Ala	
		195					200					205				
Cys	Ser	Ser	Ser	Leu	Val	Ala	Leu	His	Leu	Ala	Cys	Gln	Ala	Leu	Arg	
		210				215					220					
Ser	Gly	Glu	Cys	Thr	Met	Ala	Leu	Ala	Gly	Gly	Ala	Ser	Val	Met	Ala	
225					230					235					240	
Thr	Pro	Phe	Val	Phe	Thr	Glu	Phe	Ser	Arg	Gln	Arg	Gly	Leu	Ala	Ala	
				245					250					255		
Asp	Gly	Arg	Cys	Lys	Ala	Phe	Ser	Ala	Ala	Ala	Asp	Gly	Thr	Gly	Trp	
			260					265					270			
Ser	Glu	Gly	Val	Gly	Met	Leu	Leu	Val	Glu	Arg	Leu	Ser	Asp	Ala	Arg	
		275					280					285				
Arg	Asn	Gly	His	Arg	Val	Leu	Ala	Val	Val	Arg	Gly	Ser	Ala	Val	Asn	
		290				295					300					
Gln	Asp	Gly	Ala	Ser	Asn	Gly	Leu	Thr	Ala	Pro	Asn	Gly	Arg	Ser	Gln	
305					310					315					320	
Val	Lys	Val	Ile	Arg	Gln	Ala	Leu	Ala	Asn	Ala	His	Leu	Ser	Pro	Ala	
				325					330					335		
Asp	Val	Asp	Ala	Val	Glu	Ala	His	Gly	Thr	Gly	Thr	Thr	Leu	Gly	Asp	
			340					345					350			
Pro	Ile	Glu	Ala	Gln	Ala	Leu	Val	Glu	Ala	Tyr	Gly	Gln	Asp	Arg	Pro	
		355					360					365				
Asn	Gly	Arg	Pro	Leu	Trp	Leu	Gly	Thr	Leu	Lys	Ser	Asn	Ile	Gly	His	
		370				375					380					
Ser	Met	Ala	Ala	Ala	Gly	Val	Gly	Gly	Val	Ile	Lys	Met	Val	Met	Ala	
385					390					395					400	
Leu	Arg	Asn	Gly	Leu	Leu	Pro	Arg	Thr	Leu	His	Val	Asp	Glu	Pro	Ser	
				405					410					415		

Pro	His	Val	Asp	Trp	Ser	Ala	Gly	Ala	Val	Gln	Leu	Leu	Thr	Glu	Thr	420	425	430	
Val	Pro	Trp	Pro	Gly	Gly	Glu	Gly	Arg	Leu	Arg	Arg	Ala	Gly	Val	Ser	435	440	445	
Ser	Phe	Gly	Val	Ser	Gly	Thr	Asn	Ala	His	Val	Ile	Leu	Glu	Glu	Ala	450	455	460	
Pro	Ala	His	Asn	Ile	Pro	Ser	Asp	Thr	Pro	Ala	Asp	Asp	Val	Pro	Gly	465	470	475	480
Glu	Ser	Ala	Ala	Asp	Glu	Asp	Ala	Gly	Ser	Gly	Asp	Glu	Ala	Ala	Ala	485	490	495	
Gly	Ser	Pro	Gly	Val	Trp	Pro	Trp	Leu	Val	Ser	Ala	Lys	Ser	Gln	Pro	500	505	510	
Ala	Leu	Arg	Ala	Gln	Ala	Gln	Ala	Leu	His	Ala	His	Leu	Thr	Asp	His	515	520	525	
Pro	Gly	Leu	Asp	Leu	Ala	Asp	Val	Gly	Tyr	Thr	Leu	Ala	His	Ala	Arg	530	535	540	
Ala	Val	Phe	Asp	His	Arg	Ala	Thr	Leu	Ile	Ala	Ala	Asp	Arg	Asp	Thr	545	550	555	560
Phe	Leu	Gln	Ala	Leu	Gln	Ala	Leu	Ala	Ala	Gly	Glu	Pro	His	Pro	Ala	565	570	575	
Val	Ile	His	Ser	Ser	Ala	Pro	Gly	Gly	Thr	Gly	Thr	Gly	Glu	Ala	Ala	580	585	590	
Gly	Lys	Thr	Ala	Phe	Ile	Cys	Ser	Gly	Gln	Gly	Thr	Gln	Arg	Pro	Gly	595	600	605	
Met	Ala	His	Gly	Leu	Tyr	His	Thr	His	Pro	Val	Phe	Ala	Ala	Ala	Leu	610	615	620	
Asn	Asp	Ile	Cys	Thr	His	Leu	Asp	Pro	His	Leu	Asp	His	Pro	Leu	Leu	625	630	635	640
Pro	Leu	Leu	Thr	Gln	Asp	Pro	Asn	Thr	Gln	Asp	Thr	Thr	Thr	Leu	Glu	645	650	655	
Glu	Ala	Ala	Ala	Leu	Leu	Gln	Gln	Thr	Arg	Tyr	Ala	Gln	Pro	Ala	Leu	660	665	670	
Phe	Ala	Phe	Gln	Val	Ala	Leu	His	Arg	Leu	Leu	Thr	Asp	Gly	Tyr	His	675	680	685	
Ile	Thr	Pro	His	Tyr	Tyr	Ala	Gly	His	Ser	Leu	Gly	Glu	Ile	Thr	Ala	690	695	700	
Ala	His	Leu	Ala	Gly	Ile	Leu	Thr	Leu	Thr	Asp	Ala	Thr	Thr	Leu	Ile	705	710	715	720
Thr	Gln	Arg	Ala	Thr	Leu	Met	Gln	Thr	Met	Pro	Pro	Gly	Thr	Met	Thr	725	730	735	

Thr	Leu	His	Thr	Thr	Pro	His	His	Ile	Thr	His	His	Leu	Thr	Ala	His	740	745	750
Glu	Asn	Asp	Leu	Ala	Ile	Ala	Ala	Ile	Asn	Thr	Pro	Thr	Ser	Leu	Val	755	760	765
Ile	Ser	Gly	Thr	Pro	His	Thr	Val	Gln	His	Ile	Thr	Thr	Leu	Cys	Gln	770	775	780
Gln	Gln	Gly	Ile	Lys	Thr	Lys	Thr	Leu	Pro	Thr	Asn	His	Ala	Phe	His	785	790	795
Ser	Pro	His	Thr	Asn	Pro	Ile	Leu	Asn	Gln	Leu	His	Gln	His	Thr	Gln	805	810	815
Thr	Leu	Thr	Tyr	His	Pro	Pro	His	Thr	Pro	Leu	Ile	Thr	Ala	Asn	Thr	820	825	830
Pro	Pro	Asp	Gln	Leu	Leu	Thr	Pro	His	Tyr	Trp	Thr	Gln	Gln	Ala	Arg	835	840	845
Asn	Thr	Val	Asp	Tyr	Ala	Thr	Thr	Thr	Gln	Thr	Leu	His	Gln	His	Gly	850	855	860
Val	Thr	Thr	Tyr	Ile	Glu	Leu	Gly	Pro	Asp	Asn	Thr	Leu	Thr	Thr	Leu	865	870	875
Thr	His	Asp	Asn	Leu	Pro	Asn	Thr	Pro	Thr	Thr	Thr	Leu	Thr	Leu	Thr	885	890	895
His	Pro	His	His	His	Pro	Gln	Thr	His	Leu	Leu	Thr	Asn	Leu	Ala	Lys	900	905	910
Thr	Thr	Thr	Thr	Trp	His	Pro	His	His	Tyr	Thr	His	His	His	Asn	Gln	915	920	925
Pro	His	Thr	His	Thr	His	Leu	Asp	Leu	Pro	Thr	Tyr	Pro	Phe	Gln	His	930	935	940
His	His	Tyr	Trp	Leu	Gln	Pro	Pro	Gly	Lys	Pro	Ser	Asp	Pro	Ser	Pro	945	950	955
Ser	Glu	Gly	Arg	Glu	Gln	Ala	Thr	Thr	Pro	Ser	Thr	Pro	Leu	Arg	Asp	965	970	975
Val	Leu	Val	Gly	Lys	Ser	Pro	Gln	Glu	Arg	Asp	Glu	Glu	Leu	Leu	Arg	980	985	990
Leu	Val	Arg	Thr	His	Ala	Ala	Ala	Val	Leu	Gly	His	Ala	Thr	Pro	Glu	995	1000	1005
Val	Ile	Val	Pro	Asn	Lys	Ala	Phe	Lys	Glu	Leu	Gly	Phe	Asp	Ser	Leu	1010	1015	1020
Ala	Ala	Ile	Gln	Leu	Arg	Asn	Arg	Leu	Leu	Ala	Asp	Val	Asp	Leu	Pro	1025	1030	1035
Leu	Pro	Ala	Thr	Leu	Ile	Phe	Asp	Tyr	Pro	Thr	Pro	Met	Ala	Leu	Cys	1045	1050	1055

Gln Phe Leu Arg Ala Ala Ile Val Gly Ala Asp Thr Gly Thr Thr Thr
1060 1065 1070

Arg Leu Pro Leu Thr Ala Val Pro Ala Asp Glu Pro Ile Ala Ile Val
1075 1080 1085

Gly Met Ala Cys Arg Tyr Pro Gly Asp Val Arg Thr Val Asp Asp Leu
1090 1095 1100

Trp Gln Val Val Ser Gly Gly His Asp Ala Ile Gly Gly Phe Pro Thr
1105 1110 1115 1120

Asn Arg Gly Trp Asp Leu Asp Thr Leu Tyr Asn Pro Asp Pro Asp His
1125 1130 1135

His Gly Thr Ser Tyr Thr Arg Ser Gly Gly Phe Leu Tyr Asp Ala Gly
1140 1145 1150

Asn Phe Asp Pro Asp Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala
1155 1160 1165

Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Thr Ala Trp Glu Ser Ile
1170 1175 1180

Glu His Ala Cys Ile Asn Pro Asp Ser Leu Arg Gly Thr Pro Thr Gly
1185 1190 1195 1200

Val Phe Ala Gly Leu Thr Tyr His Asp Tyr Ala Ala Arg Phe Pro Thr
1205 1210 1215

Ala Pro Ala Gly Phe Glu Gly Tyr Leu Gly His Gly Ser Ala Gly Ser
1220 1225 1230

Ile Ala Ser Gly Arg Val Ala Tyr Ala Leu Gly Leu Glu Gly Pro Ala
1235 1240 1245

Leu Thr Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu
1250 1255 1260

Ala Cys Gln Ala Leu Arg Ser Gly Glu Cys Ser Met Ala Leu Ala Gly
1265 1270 1275 1280

Gly Val Thr Val Met Ser Thr Pro Ala Gly Phe Val Glu Phe Ser Arg
1285 1290 1295

Gln Arg Gly Leu Ala Val Asp Gly Arg Cys Lys Ala Phe Ser Ala Ala
1300 1305 1310

Ala Asp Gly Thr Gly Trp Gly Glu Gly Val Gly Met Leu Leu Val Glu
1315 1320 1325

Arg Leu Ser Asp Ala Arg Arg Leu Gly His Arg Ile Leu Ala Val Val
1330 1335 1340

Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala
1345 1350 1355 1360

Pro Asn Gly Pro Ser Gln Glu Arg Val Ile Arg Leu Ala Leu Ala Asn
1365 1370 1375

Ala	Asp	Leu	Thr	Pro	Ala	Asp	Val	Asp	Ala	Val	Glu	Ala	His	Gly	Thr	1380	1385	1390
Gly	Thr	Thr	Leu	Gly	Asp	Pro	Ile	Glu	Ala	Gln	Ala	Leu	Leu	Ala	Thr	1395	1400	1405
Tyr	Gly	Gln	Asp	Arg	Pro	Gly	Asn	Glu	Pro	Leu	Trp	Leu	Gly	Ser	Met	1410	1415	1420
Lys	Ser	Asn	Ile	Gly	His	Ala	Gln	Ala	Ala	Ala	Gly	Val	Gly	Gly	Val	1425	1430	1435
Ile	Lys	Met	Val	Met	Ala	Leu	Arg	Asn	Gly	Leu	Leu	Pro	Arg	Thr	Leu	1445	1450	1455
His	Val	Asp	Glu	Pro	Ser	Pro	His	Val	Asp	Trp	Ser	Ala	Gly	Ala	Val	1460	1465	1470
Gln	Leu	Leu	Thr	Glu	Thr	Val	Pro	Trp	Pro	Gly	Gly	Glu	Gly	Arg	Leu	1475	1480	1485
Arg	Arg	Ala	Gly	Val	Ser	Ser	Phe	Gly	Val	Ser	Gly	Thr	Asn	Ala	His	1490	1495	1500
Val	Ile	Leu	Glu	Glu	Ala	Pro	Ala	His	Asn	Ile	Pro	Ser	Asp	Thr	Pro	1505	1510	1515
Ala	Asp	Asp	Ala	Pro	Gly	Glu	Ala	Ala	Ala	Asp	Asp	Val	Pro	Gly	Glu	1525	1530	1535
Ala	Ala	Gly	Asp	Asp	Ala	Gly	Thr	Gly	Gly	Glu	Ala	Thr	Gly	Pro	Ala	1540	1545	1550
Ala	Gly	Ser	Pro	Gly	Val	Trp	Pro	Trp	Leu	Val	Ser	Ala	Lys	Ser	Gln	1555	1560	1565
Pro	Ala	Leu	Arg	Ala	Gln	Ala	Gln	Ala	Leu	His	Ala	His	Leu	Thr	Asp	1570	1575	1580
His	Pro	Gly	Leu	Asp	Leu	Ala	Asp	Val	Gly	Tyr	Thr	Leu	Ala	His	Ala	1585	1590	1595
Arg	Ala	Val	Phe	Asp	His	Arg	Ala	Thr	Leu	Ile	Ala	Ala	Asp	Arg	Asp	1605	1610	1615
Thr	Phe	Leu	Gln	Ala	Leu	Gln	Ala	Leu	Ala	Ala	Gly	Glu	Pro	His	Pro	1620	1625	1630
Ala	Val	Ile	His	Ser	Ser	Ala	Pro	Gly	Gly	Thr	Gly	Thr	Gly	Glu	Ala	1635	1640	1645
Ala	Gly	Lys	Thr	Ala	Phe	Ile	Cys	Ser	Gly	Gln	Gly	Thr	Gln	Arg	Pro	1650	1655	1660
Gly	Met	Ala	His	Gly	Leu	Tyr	His	Thr	His	Pro	Val	Phe	Ala	Ala	Ala	1665	1670	1675
Leu	Asn	Asp	Ile	Cys	Thr	His	Leu	Asp	Pro	His	Leu	Asp	His	Pro	Leu	1685	1690	1695

Leu Pro Leu Leu Thr Gln Asp Pro Asn Thr Gln Asp Thr Thr Thr Leu
 1700 1705 1710
 Glu Glu Ala Ala Ala Leu Leu Gln Gln Thr Pro Tyr Ala Gln Pro Ala
 1715 1720 1725
 Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr Asp Gly Tyr
 1730 1735 1740
 His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly Glu Ile Thr
 1745 1750 1755 1760
 Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala Thr Thr Leu
 1765 1770 1775
 Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro Gly Thr Met
 1780 1785 1790
 Thr Thr Leu His Thr Thr Pro His His Ile Thr His His Leu Thr Ala
 1795 1800 1805
 His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro Thr Ser Leu
 1810 1815 1820
 Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr Thr Leu Cys
 1825 1830 1835 1840
 Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Lys Asn Ala Phe
 1845 1850 1855
 His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His Gln His Thr
 1860 1865 1870
 Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile Thr Ala Asn
 1875 1880 1885
 Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr Gln Gln Ala
 1890 1895 1900
 Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr Leu His Gln His
 1905 1910 1915 1920
 Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr Leu Thr Thr
 1925 1930 1935
 Leu Thr His His Asn Leu Pro Asn Thr Pro Thr Thr Thr Leu Thr Leu
 1940 1945 1950
 Thr His Pro His His His Pro Gln Thr His Leu Leu Thr Asn Leu Ala
 1955 1960 1965
 Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr His His His Asn
 1970 1975 1980
 Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr Pro Phe Gln
 1985 1990 1995 2000
 His Gln His Tyr Trp Leu Glu Ser Thr Gln Pro Gly Ala Gly Ser Gly
 2005 2010 2015

Ser Gly Ser Gly Ser Gly Arg Ala Gly Thr Ala Gly Gly Thr Ala Glu
2020 2025 2030

Val Glu Ser Arg Phe Trp Asp Ala Val Ala Arg Gln Asp Leu Glu Thr
2035 2040 2045

Val Ala Thr Thr Leu Ala Val Pro Pro Ser Ala Gly Leu Asp Thr Val
2050 2055 2060

Val Pro Ala Leu Ser Ala Trp His Arg His Gln His Asp Gln Ala Arg
2065 2070 2075 2080

Ile Asn Thr Trp Thr Tyr Gln Glu Thr Trp Lys Pro Leu Thr Leu Pro
2085 2090 2095

Thr Thr His Gln Pro His Gln Thr Trp Leu Ile Ala Ile Pro Glu Thr
2100 2105 2110

Gln Thr His His Pro His Ile Thr Asn Ile Leu Thr Asn Leu His His
2115 2120 2125

His Gly Ile Thr Pro Ile Pro Leu Thr Leu Asn His Thr His Thr Asn
2130 2135 2140

Pro Gln His Leu His His Thr Arg Gln Gln Ala Gln Asn His Thr Thr
2145 2150 2155 2160

Gly Pro Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu Asp Glu Thr Pro
2165 2170 2175

His Pro His His Pro His Thr Pro Thr Gly Thr Leu Leu Asn Leu Thr
2180 2185 2190

Leu Thr Gln Thr His Thr Gln Thr His Pro Pro Thr Pro Leu Trp Tyr
2195 2200 2205

Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp Pro Leu Thr His
2210 2215 2220

Pro Thr Gln Ala Gln Thr Trp Gly Leu Ala Arg Thr Thr Leu Leu Glu
2225 2230 2235 2240

His Pro Thr His Thr Ala Gly Ile Ile Asp Leu Pro Thr Thr Pro Thr
2245 2250 2255

Pro His Thr Leu His His Leu Thr Gln Thr Leu Thr Gln Pro His His
2260 2265 2270

Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His Thr Arg Arg Leu
2275 2280 2285

Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro Thr Pro Thr Pro
2290 2295 2300

His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala Leu Ala Thr His
2305 2310 2315 2320

Leu Thr His His Leu Thr Thr His Gln Pro Thr Gln His Leu Leu Leu
2325 2330 2335

Thr	Ser	Arg	Thr	Gly	Pro	His	Thr	Pro	His	Ala	Gln	His	Leu	Thr	Thr	2340	2345	2350
Gln	Leu	Gln	Gln	Lys	Gly	Ile	His	Leu	Thr	Ile	Thr	Thr	Cys	Asp	Thr	2355	2360	2365
Ser	Asn	Pro	Asp	Gln	Leu	Gln	Gln	Leu	Leu	Asn	Thr	Ile	Pro	Pro	Gln	2370	2375	2380
His	Pro	Leu	Thr	Thr	Val	Ile	His	Thr	Ala	Gly	Ile	Leu	Asp	Asp	Ala	2385	2390	2395 2400
Thr	Leu	Thr	Asn	Leu	Thr	Pro	Thr	Gln	Leu	Asn	Asn	Val	Leu	Arg	Ala	2405	2410	2415
Lys	Ala	His	Ser	Ala	His	Leu	Leu	His	Gln	Leu	Thr	Gln	His	Thr	Pro	2420	2425	2430
Leu	Asn	Ala	Phe	Val	Leu	Tyr	Ser	Ser	Ala	Ala	Ala	Thr	Phe	Gly	Ala	2435	2440	2445
Pro	Gly	Gln	Ala	Asn	Tyr	Ala	Ala	Ala	Asn	Ala	Tyr	Leu	Asp	Ala	Leu	2450	2455	2460
Ala	His	His	Arg	His	Thr	His	His	Leu	Pro	Ala	Thr	Ser	Ile	Ala	Trp	2465	2470	2475 2480
Gly	Thr	Trp	Gln	Gly	Asn	Gly	Leu	Ala	Thr	Gly	Gln	Val	Ser	Glu	His	2485	2490	2495
Leu	Arg	Arg	Arg	Gly	Met	Phe	Ala	Met	Pro	Pro	Glu	Leu	Ala	Val	Thr	2500	2505	2510
Ala	Val	Asp	Gly	Ala	Ile	Ala	Ser	Gly	Arg	Pro	Ser	Leu	Leu	Val	Ala	2515	2520	2525
Asp	Ile	Asp	Trp	Lys	Lys	Leu	Gly	Pro	Val	Leu	Ser	Ser	Lys	Ser	Ser	2530	2535	2540
Val	Leu	Leu	Glu	Asp	Leu	Pro	Gln	Ala	Gln	Gly	Thr	Glu	Glu	Ala	Arg	2545	2550	2555 2560
Ser	Thr	Val	Glu	Gln	Thr	Glu	Ser	Thr	Asn	Leu	Arg	Gln	Leu	Leu	Met	2565	2570	2575
Gly	Arg	Ser	Arg	Ser	Glu	Gln	Glu	Glu	Glu	Leu	Leu	Ser	Leu	Val	Arg	2580	2585	2590
Ile	His	Ser	Ala	Ala	Val	Leu	Gly	Arg	Asp	Asp	Ser	Glu	Ala	Ile	Pro	2595	2600	2605
Pro	Gly	Arg	Leu	Phe	Arg	Asp	Leu	Gly	Phe	Asp	Ser	Leu	Ala	Ala	Val	2610	2615	2620
Glu	Leu	Arg	Asn	His	Leu	Ala	Ala	Gln	Thr	Glu	Leu	Ala	Leu	Pro	Thr	2625	2630	2635 2640
Thr	Leu	Val	Phe	Asp	Tyr	Pro	Ser	Pro	Thr	Lys	Leu	Ala	Gln	Phe	Leu	2645	2650	2655

Leu	Ser	Glu	Ile	Ala	Glu	Phe	Gln	Pro	Asp	Asn	Ser	Thr	Pro	Leu	Pro	
2660						2665						2670				
Arg	Pro	Arg	Ala	Glu	Leu	Asp	Glu	Pro	Ile	Ala	Ile	Val	Gly	Met	Ala	
2675						2680						2685				
Cys	Arg	Phe	Pro	Gly	Gly	Val	Thr	Ser	Ala	Asp	Asp	Phe	Trp	Asp	Leu	
2690						2695						2700				
Ile	Ser	Ser	Glu	Gln	Asp	Ala	Ile	Gly	Gly	Phe	Pro	Thr	Asp	Arg	Gly	
2705						2710						2715				
Trp	Asp	Leu	Asp	Thr	Leu	Tyr	Asp	Pro	Asp	Pro	Asp	His	Pro	Gly	Thr	
			2725						2730						2735	
Cys	Tyr	Thr	Arg	Asn	Gly	Gly	Phe	Leu	Tyr	Asp	Ala	Gly	His	Phe	Asp	
			2740						2745						2750	
Ala	Glu	Phe	Phe	Gly	Ile	Ser	Pro	Arg	Glu	Ala	Leu	Ala	Met	Asp	Pro	
			2755						2760						2765	
Gln	Gln	Arg	Leu	Leu	Leu	Glu	Thr	Ala	Trp	Glu	Thr	Ile	Glu	His	Ala	
2770						2775						2780				
Gly	Ile	Asn	Pro	His	Thr	Leu	His	Gly	Thr	Pro	Thr	Gly	Val	Phe	Thr	
2785						2790						2795				
Gly	Thr	Asn	Gly	Gln	Asp	His	Ala	Ala	His	Ile	Arg	Gln	Ala	Pro	Ser	
			2805						2810						2815	
Gly	Thr	Glu	Gly	Phe	Val	Leu	Thr	Gly	Ala	Ala	Thr	Ser	Ile	Ala	Ser	
			2820						2825						2830	
Gly	Arg	Ile	Ser	Tyr	Ile	Leu	Gly	Leu	Glu	Gly	Pro	Ala	Val	Thr	Leu	
2835						2840						2845				
Asp	Thr	Ala	Cys	Ser	Ser	Ser	Leu	Val	Ala	Leu	His	Leu	Ala	Cys	Gln	
2850						2855						2860				
Ser	Leu	Arg	Ser	Gly	Glu	Cys	Thr	Met	Ala	Leu	Ala	Gly	Gly	Ala	Thr	
2865						2870						2875				
Val	Met	Thr	Thr	Pro	Ile	Thr	Phe	Thr	Glu	Phe	Ala	Arg	Gln	Arg	Gly	
			2885						2890						2895	
Leu	Ala	Pro	Asp	Gly	Arg	Cys	Lys	Ala	Phe	Ser	Ala	Ala	Ala	Asp	Gly	
			2900						2905						2910	
Thr	Gly	Trp	Gly	Glu	Gly	Val	Gly	Met	Leu	Leu	Val	Glu	Arg	Leu	Ser	
2915						2920						2925				
Asp	Ala	Arg	Arg	Asn	Gly	His	Arg	Val	Leu	Ala	Val	Val	Arg	Gly	Ser	
2930						2935						2940				
Ala	Val	Asn	Gln	Asp	Gly	Ala	Ser	Asn	Gly	Leu	Thr	Ala	Pro	Asn	Gly	
2945						2950						2955				
Pro	Ser	Gln	Gln	Arg	Val	Ile	Arg	Gln	Ala	Leu	Ala	Asn	Ala	Asp	Leu	
			2965						2970						2975	

09044660 09240

Thr	Pro	Ala	Asp	Val	Asp	Ala	Val	Glu	Ala	His	Gly	Thr	Gly	Thr	Thr	2980	2985	2990	
Leu	Gly	Asp	Pro	Ile	Glu	Ala	Gln	Ala	Ile	Leu	Ala	Thr	Tyr	Gly	Gln	2995	3000	3005	
Asp	Arg	Pro	Gly	Asn	Gly	Pro	Leu	Trp	Leu	Gly	Ser	Val	Lys	Ser	Asn	3010	3015	3020	
Val	Gly	His	Thr	Gln	Ala	Ala	Ala	Gly	Val	Ala	Gly	Val	Ile	Lys	Met	3025	3030	3035	3040
Val	Met	Ala	Leu	Arg	His	Arg	Thr	Leu	Pro	Pro	Thr	Leu	His	Ala	Asp	3045	3050	3055	
Glu	Pro	Ser	Pro	His	Val	Asp	Trp	Ser	Ala	Gly	Ala	Val	Gln	Leu	Leu	3060	3065	3070	
Thr	Glu	Thr	Val	Pro	Trp	Pro	Gly	Gly	Glu	Gly	Arg	Pro	Arg	Arg	Ala	3075	3080	3085	
Gly	Val	Ser	Ser	Phe	Gly	Val	Ser	Gly	Thr	Asn	Ala	His	Val	Ile	Leu	3090	3095	3100	
Glu	Glu	Ala	Pro	Ala	Asp	Asp	Val	Pro	Gly	Gly	Pro	Pro	Ala	Asp	Glu	3105	3110	3115	3120
Asp	Ala	Gly	Ser	Gly	Glu	Glu	Ala	Ala	Ala	Gly	Ser	Pro	Gly	Val	Trp	3125	3130	3135	
Pro	Trp	Leu	Val	Ser	Ala	Lys	Ser	Gln	Pro	Ala	Leu	Arg	Ala	Gln	Ala	3140	3145	3150	
Gln	Ala	Leu	His	Ala	His	Leu	Thr	Asp	His	Pro	Gly	Leu	Asp	Leu	Ala	3155	3160	3165	
Asp	Val	Gly	Tyr	Thr	Leu	Ala	His	Ala	Arg	Ala	Val	Phe	Asp	His	Arg	3170	3175	3180	
Ala	Thr	Leu	Ile	Ala	Ala	Asp	Arg	Asp	Thr	Phe	Leu	Gln	Ala	Leu	Gln	3185	3190	3195	3200
Ala	Leu	Ala	Ala	Gly	Glu	Pro	His	Pro	Ala	Val	Ile	His	Ser	Ser	Ala	3205	3210	3215	
Pro	Gly	Gly	Thr	Gly	Thr	Gly	Glu	Ala	Ala	Gly	Lys	Thr	Ala	Phe	Ile	3220	3225	3230	
Cys	Ser	Gly	Gln	Gly	Thr	Gln	Arg	Pro	Gly	Met	Ala	His	Gly	Leu	Tyr	3235	3240	3245	
His	Thr	His	Pro	Val	Phe	Ala	Ala	Ala	Leu	Asn	Asp	Ile	Cys	Thr	His	3250	3255	3260	
Leu	Asp	Pro	His	Leu	Asp	His	Pro	Leu	Leu	Pro	Leu	Leu	Thr	Gln	Asn	3265	3270	3275	3280
Asp	Asn	Asp	Asn	Asp	Asn	Glu	Asp	Ala	Ala	Ala	Leu	Leu	Gln	Gln	Thr	3285	3290	3295	

Pro Tyr Ala Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg
3300 3305 3310

Leu Leu Thr Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His
3315 3320 3325

Ser Leu Gly Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu
3330 3335 3340

Thr Asp Ala Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr
3345 3350 3355 3360

Met Pro Pro Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile
3365 3370 3375

Thr His His Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile
3380 3385 3390

Asn Thr Pro Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln
3395 3400 3405

His Ile Thr Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu
3410 3415 3420

Pro Thr Asn His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn
3425 3430 3435 3440

Gln Leu His Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr
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Pro Leu Ile Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His
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Tyr Trp Thr Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr
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Gln Thr Leu His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro
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Asp Asn Thr Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Thr Pro
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Thr Thr Thr Leu Thr Leu Thr His Pro His His His Pro Gln Thr His
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Leu Leu Thr Asn Leu Ala Lys Thr Thr Thr Trp His Pro His His
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Tyr Thr His His His Asn Gln Pro His Thr His Thr His Leu Asp Leu
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Pro Thr Tyr Pro Phe Gln His His His Tyr Trp Leu Glu Leu Pro Ser
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Ala Gln Thr Ser Pro Gly Gln Arg Arg Ser Arg Arg Ser Ala Pro Asp
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Thr Ala Glu Ser Glu Phe Trp Asp Ala Val Asn Glu Glu Asp Leu Gln
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Ser Leu Ala Glu Thr Leu Asp Ile Asp Ala Ser Ala Leu Asp Thr Val
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Val Pro Ala Leu Ser Ala Trp His Arg His Gln His Asp Gln Ala Arg
3635 3640 3645

Ile Asn Thr Trp Thr Tyr Gln Glu Thr Trp Lys Pro Leu Thr Leu Pro
3650 3655 3660

Thr Thr His Gln Pro His Gln Thr Trp Leu Ile Ala Ile Pro Glu Thr
3665 3670 3675 3680

Gln Thr His His Pro His Ile Thr Asn Ile Leu Thr Asn Leu His His
3685 3690 3695

His Gly Ile Thr Pro Ile Pro Leu Thr Val Asn His Thr His Thr Asn
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Pro Gln His Leu His His Thr Leu His His Thr Arg Gln Gln Ala Gln
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Asn His Thr Thr Gly Pro Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu
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Asp Glu Thr Pro His Pro His His Pro His Thr Pro Thr Gly Thr Leu
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Leu Asn Leu Thr Leu Pro Gln Thr His Thr Gln Thr His Pro Pro Thr
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Pro Leu Trp Tyr Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp
3780 3785 3790

Pro Leu Thr His Pro Thr Gln Ala Gln Thr Trp Gly Leu Ala Arg Thr
3795 3800 3805

Thr Leu Leu Glu His Pro Thr His Thr Ala Gly Ile Ile Asp Leu Pro
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Thr Thr Pro Thr Pro His Thr Leu His His Leu Thr Gln Thr Leu Thr
3825 3830 3835 3840

Gln Pro His His Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His
3845 3850 3855

Thr Arg Arg Leu Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro
3860 3865 3870

Thr Pro Thr Pro His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala
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Leu Ala Thr His Leu Thr His His Leu Thr Thr His Gln Pro Thr Gln
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His Leu Leu Leu Thr Ser Arg Thr Gly Pro His Thr Pro His Ala Gln
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His Leu Thr Thr Gln Leu Gln Gln Lys Gly Ile His Leu Thr Ile Thr
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Thr Cys Asp Thr Ser Asn Pro Asp Gln Leu Gln Gln Leu Leu Asn Thr
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 Val Thr Ala Ala Lys Ala Thr Gly Ala Ala Ile Leu His Glu Leu Leu
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 Ala Phe Thr Ala Arg Arg His Ser Pro Leu Ile Glu Asp Ile Pro Glu
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 Val Arg Gln Ala Ala Gln Glu Leu Glu Ala Ala Ala Ser Thr Ala Lys
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 Thr Thr Thr Ala Gln Pro Ile Ala Thr Ser Leu Arg Glu Arg Leu Ala
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 Thr Gly Ile Cys Thr Val Leu Gly Leu Arg Asn Pro Glu Gly Ile Glu
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 Gln Phe Ser Lys Glu Leu Ala Lys Glu Thr Gly Leu Pro Leu Pro Pro
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 Ser Leu Val Phe Asp Tyr Pro Thr Pro Gln Glu Cys Ala Ala His Leu
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 Arg Thr Gln Leu Val Asp Leu Asp Asp Glu Glu Asp Ala Ala Leu Ser
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Asn Ala Leu Pro Gln Val Ala His Arg Arg Thr Val Glu Asp Glu Pro
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Ile Ala Ile Ile Gly Met Ala Cys Arg Phe Pro Gly Gly Val Arg Ser
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Ala Asp Asp Leu Trp Glu Leu Leu Ala Ser Gly Lys Asp Ala Ile Gly
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Val Phe Pro Thr Asp Arg Gly Trp Asp Leu Asp Thr Leu Tyr Asp Pro
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Asp Pro Asp His Pro Gly Thr Cys Tyr Thr Arg Asn Gly Gly Phe Leu
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Tyr Gly Ala Gly His Phe Asp Ala Glu Phe Phe Gly Ile Ser Pro Arg
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Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Thr Ala
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Trp Glu Thr Ile Glu His Ala Gly Ile Asn Pro His Thr Leu His Gly
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Thr Pro Thr Gly Val Phe Ala Gly Ile Asn Ala Gln Asp His Ala Ala
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His Ile Arg Gln Ser Arg Asp Val Glu Thr Ile Glu Gly Tyr Ala Leu
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Thr Gly Ser Ser Gly Ser Val Ala Ser Gly Arg Val Ala Tyr Thr Leu
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Gly Leu Glu Gly Pro Ala Val Ser Val Asp Thr Ala Cys Ser Ser Ser
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Leu Val Ala Leu His Trp Ala Ala Gln Ala Leu Arg Ala Gly Glu Cys
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Ser Met Ala Leu Ala Gly Gly Val Thr Val Met Ser Ser Pro Gly Thr
4465 4470 4475 4480

Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala Asp Gly Arg Cys
4485 4490 4495

Lys Ala Tyr Ser Ala Ala Ala Asp Gly Thr Gly Trp Ala Glu Gly Val
4500 4505 4510

Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly His
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Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala
4530 4535 4540

Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln Gln Arg Val Ile
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Arg Gln Ala Leu Ala Asn Ala Gly Leu Thr Pro Ala Asp Val Asp Ala
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Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala
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 Gln Ala Leu Leu Ala Ala Tyr Gly Gln His Arg Pro His His Arg Pro
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 Cys Thr Asp Thr Gly Leu Arg Ala Lys Arg Ile Pro Val Asp Tyr Ala
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 Leu Thr Asp Asp Gly His Arg Ala Phe Ile Glu Ile Ser Pro His Pro
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 Thr Leu Val Pro Ala Ile Glu Asp Thr Thr Glu Asn Thr Thr Glu Asn
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 Phe Leu Thr Ala Leu Ala His Thr His Thr Thr Gly Ile Gly Thr Pro
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 Arg Ser Pro Gln His Gly Asn Ala Val Ala Leu Thr Ala Ala Asp Glu
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Pro His Leu Pro Gly Leu Thr Glu His Glu His Val Thr Ala Tyr Asp
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Thr Gly Val Leu Gly Arg Leu Val Ala Arg His Leu Val Glu Ala His
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Glu Val Val Ala Cys Asp Ala Ala Asp Arg Gln Gln Leu Ala Asp Leu
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Ala Gly Ile Leu Asp Asp Gly Val Ile Thr Ser Leu Ser Pro Glu Arg
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 Thr Gly His Leu Asp Val Asp Asp His Ala Arg Ile Ser Arg Ala Gly
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 Arg Ser His Val Ala Ala Val Leu Gly His Ser Gly Ala Asp Gly Ile
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 Asp Ala Ser Arg Ala Phe Arg Glu Leu Gly Phe Asp Ser Leu Thr Ala
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Gly Pro Glu Asp Ala Pro Pro Ser Gly Gln Asp Thr Pro Ala Pro Val
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Ser Ile Asp Glu Met Asp Ile Asp Asp Leu Met Asp Leu Ala His Gly
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Ser Ser Arg Asn Arg Thr His His Thr His Glu Glu Thr Ala
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<211> 4881

<212> PRT

<213> Streptomyces avermitilis

<400> 5

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20 25 30

Gln Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Phe Pro Gly Gly
35 40 45

Val Glu Ser Ala Glu Asp Phe Trp Glu Leu Ile Ala Ser Gly Arg Asp
50 55 60

Ala Val Gly Glu Phe Pro Val Asp Arg Gly Trp Asp Val Glu Ala Phe
65 70 75 80

Tyr Asp Pro Glu Pro Gly Arg Ala Gly Ser Ser Tyr Thr Arg Arg Gly
85 90 95

Gly Phe Leu Glu Gly Ala Ala Glu Phe Asp Ala Gly Phe Phe Gly Ile
100 105 110

Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Met Leu
115 120 125

Glu Val Ser Trp Glu Ala Leu Glu Arg Ala Gly Ile Asp Pro Ala Thr
130 135 140

Leu Arg Gly Ser Arg Thr Gly Val Phe Ala Gly Leu Met Ser Gln Asp
145 150 155 160

Tyr Ala Thr Arg Leu Leu Ser Val Pro Asp Asp Leu Ala Gly Tyr Leu
165 170 175

Gly Asn Gly Asn Ala Gly Ser Ile Leu Ser Gly Arg Val Ala Tyr Thr
180 185 190

Phe Gly Phe Glu Gly Pro Ala Val Thr Val Asp Thr Ala Cys Ser Ser
195 200 205

Ser Leu Val Ala Leu His Leu Ala Cys Gln Ser Leu Arg Thr Gly Glu
210 215 220

Ser	Ser	Phe	Ala	Leu	Ala	Gly	Gly	Val	Thr	Val	Met	Ser	Thr	Pro	Gly
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Met	Phe	Val	Glu	Phe	Ser	Arg	Gln	Arg	Gly	Leu	Ser	Pro	Asp	Gly	Arg
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Cys	Lys	Ala	Tyr	Ala	Ser	Ala	Ala	Asp	Gly	Thr	Gly	Met	Ser	Glu	Gly
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Val	Gly	Ile	Leu	Leu	Leu	Glu	Arg	Leu	Ser	Glu	Ala	Glu	Arg	Arg	Gly
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His	Arg	Val	Leu	Ala	Val	Val	Arg	Gly	Ser	Ala	Val	Asn	Gln	Asp	Gly
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Ile	Arg	Gln	Ala	Leu	Ala	Cys	Ala	Gly	Leu	Ser	Val	Ala	Asp	Val	Asp
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Val	Val	Glu	Gly	His	Gly	Thr	Gly	Thr	Thr	Leu	Gly	Asp	Pro	Ile	Glu
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Ala	Gln	Ala	Leu	Leu	Ala	Thr	Tyr	Gly	Gln	Arg	Ala	Gly	Asp	Thr	Pro
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Val	Trp	Leu	Gly	Ser	Val	Lys	Ser	Asn	Ile	Gly	His	Ala	Gln	Ala	Ala
	370					375					380				
Ala	Gly	Val	Ala	Gly	Val	Ile	Lys	Met	Val	Met	Ala	Leu	Arg	Ala	Gly
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Val	Leu	Pro	Arg	Thr	Leu	His	Val	Asp	Glu	Pro	Ser	Ser	Gln	Val	Asp
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Trp	Ser	Ser	Gly	Ser	Val	Arg	Val	Leu	Ala	Asp	Glu	Val	Glu	Trp	Pro
			420					425					430		
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Gly	Ser	Gly	Val	Val	Pro	Trp	Val	Val	Ser	Ala	Arg	Ser	Glu	Leu	Ala
				485					490					495	
Leu	Arg	Gly	Gln	Ala	Arg	Arg	Leu	Arg	Gly	Val	Val	Ala	Val	Gly	Gly
			500					505					510		
Gly	Ala	Asp	Gly	Val	Gly	Val	Ser	Pro	Ala	Gly	Val	Gly	Arg	Ala	Leu
		515					520					525			
Val	Ser	Glu	Arg	Ser	Val	Phe	Glu	His	Arg	Ala	Val	Val	Val	Ala	Glu
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Asp	Arg	Asp	Glu	Phe	Leu	His	Ala	Leu	Asp	Ala	Leu	Ala	Gly	Gly	Arg	
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Pro	Val	Pro	Gly	Val	Val	Glu	Gly	Arg	Thr	Thr	Ser	Gly	Glu	Leu	Ala	
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Val	Leu	Phe	Ala	Gly	Gln	Gly	Thr	Gln	Arg	Ala	Gly	Met	Gly	Arg	Glu	
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Leu	Tyr	Glu	Ala	Tyr	Pro	Val	Phe	Ala	Gln	Ala	Ile	Asp	Glu	Ile	Cys	
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Ala	Glu	Ala	Asp	Thr	Ala	Arg	Thr	Asp	Pro	Gly	Ala	Pro	Gly	Leu	Arg	
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Asp	Val	Leu	Phe	Ala	Pro	Gln	Asp	Ser	Pro	Glu	Gly	Arg	Leu	Ile	Glu	
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Asp	Thr	Gly	Phe	Ala	Gln	Pro	Ala	Leu	Phe	Ala	Phe	Glu	Val	Ala	Leu	
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Phe	Arg	Leu	Leu	Glu	Thr	Trp	Gly	Leu	Thr	Pro	Asp	Tyr	Val	Leu	Gly	
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His	Ser	Val	Gly	Glu	Leu	Ala	Ala	Ala	His	Val	Ala	Gly	Met	Leu	Cys	
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Ala	Val	Asn	Gly	Pro	Arg	Ser	Ile	Val	Leu	Ser	Gly	Asp	Glu	Asp	Ala	
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Val	Leu	Asp	Leu	Ala	Gln	Gln	Trp	Ala	Ala	Arg	Gly	Arg	Arg	Thr	Arg	
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Arg	Leu	Arg	Thr	Ser	His	Ala	Phe	His	Ser	Pro	His	Met	Asp	Ala	Met	
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785					790					795					800	
Arg	Ile	Pro	Val	Val	Ser	Asn	Val	Thr	Gly	Ala	Pro	Leu	Pro	Ala	Glu	
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Arg	Phe	Ala	Asp	Gly	Ile	Ser	Trp	Leu	Gln	Glu	Gln	Gly	Val	Thr	Thr	
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Cys	Leu	Glu	Ile	Gly	Pro	Asp	Gly	Thr	Leu	Ser	Ala	Leu	Ala	Gln	Asp	
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 Pro Glu Ala Arg Ser Val Met Thr Ala Leu Ala Glu Leu Phe Val Ala
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 Gly Thr Ala Val Glu Trp Ala Gly Val Phe Glu Gly Thr Ala Arg Glu
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 Val Gly Asp Gly Cys Gly Val Glu Leu Pro Thr Tyr Ala Phe Glu Arg
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 Glu Arg Phe Trp Leu Asp Val Glu Glu Gly Ser Ala Gly Gly Ser Gly
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 Val Ser Gly Met Trp Gly Gly Pro Leu Trp Glu Ala Val Glu Cys Gly
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 Val Ser Gly Gly Gly Val Gly Gly Leu Ser Gly Ala Trp Leu Val Val
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 Ser Arg Glu Val Leu Ala Gly His Leu Arg Glu Ala Val Asp Gly Glu
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 Ala Val Gly Gly Val Val Ser Leu Val Gly Trp Gly Ser Gly Val Val
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 Gln Ala Gly Val Ala Ser Val Gly Leu Val Gln Ala Leu Gly Asp Val
 1090 1095 1100
 Gly Val Gly Ala Arg Leu Trp Cys Val Thr Gly Gly Ala Val Ser Val
 1105 1110 1115 1120
 Gly Gly Arg Asp Ala Val Trp Gly Pro Ala Ser Gly Val Val Trp Gly
 1125 1130 1135
 Leu Gly Arg Val Val Gly Ala Glu Ala Pro Asp Arg Trp Gly Gly Leu
 1140 1145 1150
 Val Asp Val Pro Glu Leu Val Asp Glu Arg Val Val Asp Gly Leu Val
 1155 1160 1165
 Gly Val Leu Ala Gly Val Gly Gly Gly Glu Ser Glu Phe Ala Val
 1170 1175 1180

Arg Ser Ser Gly Ala Phe Val Arg Arg Leu Val Arg Ala Pro Leu Glu
1185 1190 1195 1200

Glu Ala Val Ala Glu Arg Glu Trp Arg Pro Arg Gly Thr Val Leu Val
1205 1210 1215

Thr Gly Gly Thr Gly Glu Leu Gly Ala His Val Ala Arg Trp Met Ala
1220 1225 1230

Arg Arg Gly Ala Glu His Leu Leu Leu Val Ser Arg Arg Gly Glu Ser
1235 1240 1245

Ala Gln Gly Val Glu Glu Leu Arg Ala Asp Leu Met Gly Leu Gly Ala
1250 1255 1260

Arg Val Ser Val Val Ala Cys Asp Ala Ala Asp Arg Glu Ala Leu Ala
1265 1270 1275 1280

Glu Val Leu Arg Ser Ala Val Pro Ala Glu Cys Pro Leu Gly Val Val
1285 1290 1295

Val His Ala Ala Gly Val Val Asp Asp Gly Val Leu Glu Gly Leu Ser
1300 1305 1310

Ser Glu Arg Val Thr Gly Val Leu Arg Ala Lys Ala Leu Ala Ala Trp
1315 1320 1325

Asn Leu His Glu Leu Thr Arg Gly Ala Asp Leu Ser Gly Phe Val Val
1330 1335 1340

Phe Ser Ser Ala Ala Ala Thr Phe Gly Pro Ala Gly Gln Gly Ser Tyr
1345 1350 1355 1360

Ala Ala Ala Asn Ala Tyr Val Glu Ala Ile Val Arg His Arg Arg Gly
1365 1370 1375

Glu Gly Leu Pro Gly Leu Ala Val Ala Trp Gly Pro Trp Ala Gly Gly
1380 1385 1390

Gly Met Ala Glu Gly Ala Val Gly Gln Met Arg Arg Arg Gly Leu Ala
1395 1400 1405

Ala Met Thr Pro Glu Thr Ala Leu Val Ala Leu Gly Gln Ala Leu Asp
1410 1415 1420

His Asp Glu Thr Cys Val Thr Val Ala Asp Ile Asp Trp Asp Arg Phe
1425 1430 1435 1440

Thr Ala Asn Ser Leu Pro Gly Ser Arg Leu Ser Pro Leu Ile Ser Asp
1445 1450 1455

Ile Pro Glu Ala Arg Leu Ala Arg Glu Thr Thr Gly Leu Asp Thr Ala
1460 1465 1470

Thr Ala Ser Pro Asp Ser Phe Ser Ala Arg Leu Lys Ala Met Asp Thr
1475 1480 1485

Ala Glu Gln Glu Arg Ala Leu Leu Asp Leu Val Arg Thr Tyr Ala Ala
1490 1495 1500

Thr Val Leu Gly His Ser Thr Pro Thr Ala Val Arg Pro Glu Arg Ala	1505	1510	1515	1520
Phe Arg Asp Leu Gly Phe Val Ser Val Ser Ala Val Glu Leu Arg Asn	1525	1530	1535	
Arg Leu Asn Ala Val Thr Gly Leu Leu Leu Pro Thr Thr Leu Ile Phe	1540	1545	1550	
Asp Tyr Pro Thr Pro Ser Ala Leu Ala Gly Tyr Leu Lys Glu Gln Leu	1555	1560	1565	
Glu Glu Gly Ala Gly Gly Gln Arg Asp Ile Ala Pro Pro Val Pro Ala	1570	1575	1580	
Ser Arg Val Asp Val Asp Glu Pro Ile Ala Ile Val Gly Met Ala Cys	1585	1590	1595	1600
Arg Phe Pro Gly Gly Val Glu Ser Ala Glu Asp Leu Trp Glu Leu Val	1605	1610	1615	
Ala Ser Gly Arg Asp Ala Val Gly Glu Phe Pro Val Asp Arg Gly Trp	1620	1625	1630	
Asp Val Glu Ala Phe Tyr Asp Pro Glu Pro Gly Arg Ala Gly Ser Ser	1635	1640	1645	
Tyr Thr Arg Arg Gly Gly Phe Leu Glu Gly Ala Ala Glu Phe Asp Ala	1650	1655	1660	
Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln	1665	1670	1675	1680
Gln Arg Leu Met Leu Glu Val Ser Trp Glu Ala Leu Glu Arg Ala Gly	1685	1690	1695	
Ile Asp Pro Ala Thr Leu Arg Gly Ser Thr Thr Gly Val Phe Ala Gly	1700	1705	1710	
Met Cys Ser Gln Asp Tyr Ala Asp Leu Val Arg Arg Ala Thr Glu Asp	1715	1720	1725	
Leu Glu Gly Tyr Ala Met Thr Gly Leu Ser Ser Ser Val Thr Ser Gly	1730	1735	1740	
Arg Val Ala Tyr Thr Leu Gly Leu Glu Gly Pro Ala Val Thr Val Asp	1745	1750	1755	1760
Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala	1765	1770	1775	
Leu Arg Ser Gly Glu Cys Ser Leu Ala Leu Ala Gly Gly Val Thr Val	1780	1785	1790	
Met Ser Thr Pro Gly Ala Phe Val Glu Phe Ser Arg Gln Arg Gly Leu	1795	1800	1805	
Ser Pro Asp Gly Arg Cys Lys Ala Tyr Gly Ser Gly Ala Asp Gly Val	1810	1815	1820	

Gly Trp Ala Glu Gly Val Gly Val Leu Leu Val Glu Arg Leu Ser Glu			
1825	1830	1835	1840
Ala Glu Arg Arg Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala			
	1845	1850	1855
Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro			
	1860	1865	1870
Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Cys Ala Gly Leu Ser			
	1875	1880	1885
Val Ala Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr Thr Leu			
	1890	1895	1900
Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Gly			
1905	1910	1915	1920
Arg Ser Gly Glu Arg Pro Val Trp Leu Gly Ser Val Lys Ser Asn Ile			
	1925	1930	1935
Gly His Ala Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val			
	1940	1945	1950
Met Ala Leu Arg Ala Gly Val Leu Pro Arg Thr Leu His Val Asp Glu			
	1955	1960	1965
Pro Ser Ser Gln Val Asp Trp Ser Ser Gly Ser Val Arg Val Leu Ala			
	1970	1975	1980
Asp Glu Val Glu Trp Pro Gly Val Glu Gly Arg Leu Arg Arg Ala Gly			
1985	1990	1995	2000
Val Ser Ala Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu			
	2005	2010	2015
Glu Ala Ser Gly Gly Ala Asp Gly Gly Ala Gly Arg Leu Gln Glu Leu			
	2020	2025	2030
Gly Pro Gly Val Val Ser Gly Ser Gly Val Val Pro Trp Val Val Ser			
	2035	2040	2045
Ala Arg Ser Glu Leu Ala Leu Arg Gly Gln Ala Arg Arg Leu Arg Gly			
	2050	2055	2060
Val Val Ala Val Gly Gly Gly Ala Asp Gly Val Gly Val Ser Pro Ala			
2065	2070	2075	2080
Gly Val Gly Arg Ala Leu Val Ser Glu Arg Ser Val Phe Glu His Arg			
	2085	2090	2095
Ala Val Val Val Ala Glu Asp Arg Asp Glu Phe Leu His Ala Leu Asp			
	2100	2105	2110
Ala Leu Ala Glu Gly Ala Pro Thr Ala Gly Val Val Gln Gly Val Ala			
	2115	2120	2125
Gly Pro Ala Ala Asp Gly Lys Ile Ala Met Leu Phe Gly Gly Gln Gly			
	2130	2135	2140

09914236 082404
104280 93241560

Thr His Trp Glu Gly Met Ala Gln Glu Leu Leu Gly Ser Ser Pro Val
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Phe Ala Gln Gln Met Ser Asp Cys Ala Gln Ala Leu Glu Pro Tyr Leu
2165 2170 2175

Asp Trp Ser Leu Leu Asp Val Leu Arg Gly Ala Pro Asp Ala Pro Pro
2180 2185 2190

Leu Gln Arg Val Asp Val Val Gln Pro Val Leu Phe Ala Val Met Val
2195 2200 2205

Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Val His Pro Asp Ala Val
2210 2215 2220

Ala Gly His Ser Gln Gly Glu Ile Ala Ala Ala Tyr Val Ala Gly Ala
2225 2230 2235 2240

Leu Ser Leu Asp Asp Ala Ala Arg Val Thr Ala Leu Arg Ser Gln Ala
2245 2250 2255

Leu Ala Ala Leu Ala Gly Gln Gly Ala Met Ala Ser Val Gly Leu Pro
2260 2265 2270

Val Glu Lys Leu Glu Pro Arg Leu Ala Thr Trp Gly Asp Arg Leu Val
2275 2280 2285

Ile Ala Ala Val Asn Gly Ala Arg Ser Ala Val Val Ser Gly Glu Pro
2290 2295 2300

Glu Ala Val Asp Ala Leu Val Glu Glu Leu Ser His Glu Asp Val Pro
2305 2310 2315 2320

Ala Arg Arg Leu Met Val Asp Trp Ala Ser His Ser Pro Gln Val Glu
2325 2330 2335

Ala Ile Gln Gly Arg Leu Leu Glu Leu Leu Ala Pro Ile Arg Ala Arg
2340 2345 2350

Thr Gly Asp Val Pro Phe Tyr Ser Thr Val Thr Gly Glu Arg Ile Asp
2355 2360 2365

Gly Thr Glu Leu Asp Ala Asp Tyr Trp Tyr Arg Asn Leu Arg Gln Val
2370 2375 2380

Val Arg Phe Arg Asp Ala Thr Gln Ala Leu Val Arg Ala Gly His Thr
2385 2390 2395 2400

Val Phe Ile Glu Ala Cys Pro His Pro Ala Val Ala Val Gly Val Gln
2405 2410 2415

Glu Thr Leu Asp Glu Met Gly Asp Leu Asp Ser Leu Val Val Gly Ser
2420 2425 2430

Leu Arg Arg Gly Glu Gly Gly Leu Arg Arg Phe Leu Met Ser Val Ala
2435 2440 2445

Glu Leu Phe Val Gly Gly Val Ala Val Glu Trp Ser Gly Val Phe Gly
2450 2455 2460

Ser	Val	Gly	Arg	Gly	Val	Ala	Gly	Gly	Cys	Gly	Val	Glu	Leu	Pro	Thr
2465					2470				2475					2480	
Tyr	Ala	Phe	Glu	Arg	Glu	Arg	Phe	Trp	Leu	Asp	Val	Glu	Gly	Ala	Pro
			2485					2490						2495	
Arg	Gly	Ser	Gly	Val	Ser	Gly	Gln	Trp	Gly	Gly	Gln	Leu	Ser	Glu	Ala
		2500					2505					2510			
Val	Asp	Thr	Val	Arg	Gly	Gly	Met	Leu	Arg	Asp	Cys	Leu	Ala	Gly	Leu
	2515					2520					2525				
Asp	Pro	Ala	Ala	Gln	Ala	Glu	Thr	Val	Leu	Asp	Leu	Val	Leu	Thr	His
	2530				2535					2540					
Ala	Ala	Ala	Val	Leu	Gly	His	Gly	Thr	Ala	Asp	Ala	Val	Val	Pro	Glu
2545				2550					2555						2560
Arg	Ala	Phe	Arg	Asp	Leu	Gly	Phe	Asp	Ser	Leu	Thr	Ala	Val	Glu	Leu
			2565					2570						2575	
Arg	Asn	Arg	Leu	Asn	Thr	Ala	Thr	Gly	Leu	Arg	Phe	Pro	Arg	Thr	Leu
		2580					2585					2590			
Val	Phe	Asp	His	Pro	Arg	Pro	Val	Ala	Leu	Ala	Ala	His	Ile	His	Glu
	2595					2600					2605				
Gln	Leu	Ser	Gly	Gly	Ser	Pro	Thr	Thr	Gly	Thr	Ala	Leu	Ala	Leu	Ala
2610					2615						2620				
Leu	Arg	Ala	Pro	Ala	Pro	Arg	Val	Asp	Val	Asp	Glu	Pro	Ile	Ala	Ile
2625				2630				2635						2640	
Val	Gly	Met	Ala	Cys	Arg	Phe	Pro	Gly	Gly	Val	Glu	Ser	Ala	Glu	Asp
		2645					2650						2655		
Phe	Trp	Glu	Leu	Ile	Ala	Ser	Gly	Arg	Asp	Ala	Val	Gly	Glu	Phe	Pro
		2660					2665					2670			
Val	Asp	Arg	Gly	Trp	Asp	Val	Glu	Ala	Phe	Tyr	Asp	Pro	Glu	Pro	Gly
	2675				2680						2685				
Arg	Ala	Gly	Thr	Ser	Tyr	Thr	Arg	Cys	Gly	Gly	Phe	Leu	Gln	Gly	Ala
	2690				2695					2700					
Ala	Glu	Phe	Asp	Ala	Gly	Phe	Phe	Gly	Ile	Ser	Pro	Arg	Glu	Ala	Leu
2705				2710				2715						2720	
Ala	Met	Asp	Pro	Gln	Gln	Arg	Leu	Met	Leu	Glu	Val	Ser	Trp	Glu	Ala
			2725				2730						2735		
Leu	Glu	Arg	Ala	Gly	Ile	Asp	Pro	Ala	Thr	Leu	His	Gly	Ser	Thr	Thr
		2740					2745					2750			
Gly	Val	Phe	Ala	Gly	Val	Ser	Gln	Gln	Asp	Tyr	Ala	Glu	Leu	Leu	Arg
	2755					2760					2765				
Arg	Gly	Thr	Gln	Asp	His	Glu	Gly	Tyr	Ala	Leu	Thr	Gly	Val	Ser	Asn
	2770			2775						2780					

Ser Val Val Ser Gly Arg Leu Ser Tyr Thr Phe Gly Phe Glu Gly Pro
 2785 2790 2795 2800

Ala Val Thr Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His
 2805 2810 2815

Leu Ala Cys Gln Ala Leu Arg Ser Gly Glu Cys Ser Leu Ala Leu Ala
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Gly Gly Val Thr Val Met Ser Thr Pro Gly Ala Phe Val Glu Phe Ser
 2835 2840 2845

Arg Gln Arg Gly Leu Ser Pro Asp Gly Arg Cys Lys Ala Tyr Gly Ser
 2850 2855 2860

Gly Ala Asp Gly Val Gly Trp Ala Glu Gly Val Gly Val Leu Leu Val
 2865 2870 2875 2880

Glu Arg Leu Ser Glu Ala Glu Arg Arg Gly His Arg Val Leu Ala Val
 2885 2890 2895

Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr
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Ala Pro Asn Gly Pro Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala
 2915 2920 2925

Cys Ala Gly Leu Ser Val Ala Asp Val Asp Val Val Glu Gly His Gly
 2930 2935 2940

Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala
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Thr Tyr Gly Gln Gly Arg Ser Gly Glu Arg Pro Val Trp Leu Gly Ser
 2965 2970 2975

Val Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala Gly Val Ala Gly
 2980 2985 2990

Val Ile Lys Met Val Met Ala Leu Asn His Glu Leu Leu Pro Thr Ser
 2995 3000 3005

Leu His Ile Asp Glu Pro Ser Pro His Ile Asp Trp Ser Ser Gly Gly
 3010 3015 3020

Val Arg Leu Leu Thr Glu Pro Val Pro Trp Gln Gln Asn Gly Arg Pro
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Arg Arg Ala Gly Val Ser Ala Phe Gly Val Ser Gly Thr Asn Ala His
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Val Ile Ile Glu Gln Ala Pro Val Glu Ala His Val Ile Ser Glu Pro
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Val Pro Ala Glu Ala His Val Ile Val Glu Gln Ala Pro Val Glu Ala
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Pro His Val Val Asp Ala Thr Gly Pro Ala Asp Leu Thr Glu Pro Gln
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Glu Glu Ala Ala Glu Pro Glu Cys Val Ala Asp Ala Val Thr Glu Met
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Ser Ala Glu Pro Glu Cys Val Ala Asp Ala Met Ser Glu Met Ser Ala
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Glu Cys Val Ala Glu Ala Val Ser Asp Lys Ser Ala Glu Pro Glu Cys
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Val Ala Asp Ala Met Ser Asp Lys Pro Ala Leu Leu Pro Ile Pro Trp
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Leu Leu Ser Ala Lys Ser Glu Arg Ala Leu Arg Gly Gln Ala Arg Arg
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Leu Arg Gln Phe Ala Ala Arg Ala Ser Asp Ala Arg Pro Ala Asp Val
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Ala His Ala Leu Ala Ala Gln Arg Ser Val Phe Asp His Arg Ala Val
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Val Val Ala Glu Asp Arg Asp Gly Phe Leu Gln Ala Leu Asp Ala Leu
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Ala Glu Gly Arg Ser Ala Asp Gly Leu Ile Glu Gly Ser Val Gly Pro
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Arg Gly Gly His Ser Gly Arg Arg Arg Gly Lys Thr Ala Met Leu Phe
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Ala Gly Gln Gly Thr Gln Arg Val Gly Met Gly Arg Gln Leu Tyr Ala
3265 3270 3275 3280

Ala His Pro Ala Tyr Ala Asp Ala Leu Asp Gln Val Leu Ala Glu Leu
3285 3290 3295

Asp Gly His Leu Asp Gln Pro Leu Arg Pro Leu Ile His Ala Ser Ala
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Asp Leu Ala Asp Val Ala Asp Ala Ala Asp Val Leu Asp Arg Thr Arg
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Tyr Ala Gln Pro Ala Leu Phe Ala Val Gln Val Ala Leu Phe Arg His
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Leu Glu Arg Leu Gly Val Arg Ala Asp Phe Val Ala Gly His Ser Ile
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Gly Glu Leu Ala Ala Ala His Val Ala Gly Val Leu Pro Leu Ala Ala
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Ala Cys Arg Leu Val Ala Ala Arg Gly Arg Leu Met Glu Gln Leu Ala
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Pro Gly Gly Ala Met Val Ala Val Arg Ala Ser Glu Ala Glu Ala Arg
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Gln Ala Leu Asp Gly Arg Glu Ala Arg Val Ser Val Ala Ala Val Asn
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Gly Pro Ala Ser Val Val Phe Ser Gly Ala Glu Asp Glu Val Gly Asn
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Met Ala Asp Trp Phe Ala Glu Arg Gly Arg Arg Val Lys Arg Leu Arg
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Thr Gly His Ala Phe His Ser Pro Leu Met Asp Pro Met Leu Glu Glu
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Phe Gln Gln Val Ala Ala Ser Leu Thr Tyr Ser Glu Pro Ala Ile Pro
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Met Val Ser Thr Leu Thr Gly Asp Ile Val Ala Ala Gly Glu Leu Ser
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Asp Pro Glu Tyr Trp Val Arg Gln Val Arg Arg Thr Val Arg Phe Gly
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Asp Ala Ile Ser Arg Leu His Thr Asp Gly Val Arg Thr Phe Met Glu
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Leu Gly Pro Asp Gly Thr Leu Ser Ala Leu Ala Glu Glu Cys Leu Glu
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Ala Thr Ala Asp Ser His Pro Ala Asp Asp Asp Thr Gly Thr Pro Gln
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Glu Asn Leu Leu Ile Pro Leu Leu Arg Pro Asp Ser Pro Glu Pro Gly
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Thr Leu Leu Thr Gly Leu Ala Arg Leu His Thr His Gly Ala Ala Ala
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Val Asn Trp Pro Ala Ala Leu Pro Glu Arg Asp Arg Ala Arg His Leu
3605 3610 3615

Asp Leu Pro Thr Tyr Ala Phe Asp His His Arg Tyr Trp Val Asp Thr
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Ser Ala Gly His Pro Gly Asp Leu Ser Ala Ala Gly Leu Gly Thr Ala
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Gly His Pro Leu Leu Gly Ser Ala Val Ala Leu Ala Glu Ser Gln Glu
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Leu Leu Phe Thr Gly Arg Leu Ser Leu Arg Thr His Pro Trp Leu Ala
3665 3670 3675 3680

Asp His Ala Ile Phe Gly Thr Val Leu Leu Pro Gly Thr Ala Ile Leu
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Glu Leu Ala Val Arg Ala Gly Asp Glu Val Asp Cys Gly Thr Val Glu
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Glu Leu Thr Leu Arg Thr Pro Leu Val Leu Pro Glu Gln Gly Ser Val
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Ile Leu Gln Leu Ser Val Gly Ala Pro Gln Gly Pro Gln Thr Pro Glu
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Glu Pro Glu Arg Arg Thr Phe Ala Leu Tyr Ala Arg Glu Asp Asp Gly
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Leu Ser Ser Ser Ser Ala Ala Ala Thr Gly Thr Glu Trp Thr Cys His
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 Ala Thr Gly Val Leu Thr Gly Thr Ala Arg Pro Ala Glu Glu His Thr
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 Gln Glu Pro Trp Pro Pro Ala Asp Ala Ala Pro Val Asp Leu Asp Gly
 3795 3800 3805
 Trp Tyr Glu Gln Leu Ala Gly Ala Gly Leu Gly Tyr Gly Pro Val Phe
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 Val Thr Leu Pro Glu Ser Thr Glu Gly Gln Ala Ala Asp Ala Ala Arg
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 Tyr Ala Leu His Pro Ala Leu Leu Asp Ala Ala Leu His Pro Val Val
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 Leu Arg His Glu Gly Asp Ala Ala Ala Asp Gly His Gly Trp Leu Pro
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 Phe Ser Trp Thr Gly Val Thr Val Ala Ala Ser Gly Ala Ser Thr Leu
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 His Val Arg Leu Thr Val Arg Thr Asp Glu Asp Ala Val Gly Leu Leu
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 Ala Thr Asp Ala Ser Gly Arg Ile Val Ile Ser Ala Gly Ser Leu Ala
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 Phe Arg Pro Val Ser Ala Glu Gln Leu Gln Ala Ala Arg Thr Gly Tyr
 3940 3945 3950
 His Asp His Leu Phe Arg Ile Glu Trp Arg Pro Leu His Leu Pro Thr
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 Thr Pro Ala Arg Thr Ala Asp Trp Ala Leu Ile Gly Pro Gly Ala Arg
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 Arg Thr Ala Ala Val Leu Glu Arg Asn Gly Ala Ser Trp Gln Ala Tyr
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 Pro Asp Pro Ala Ala Leu Ala Glu Ala Leu Ala Ala Gly Ala Pro Ala
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Leu Gly Pro Phe Gly Asp Gly Leu Leu Leu Ala Thr Arg Leu Asp Ala
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 Ala Thr Leu His Ala Gln Ala Thr Ala Gly Ala Leu Pro Arg Ile Leu
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 His Gly Leu Ile Arg Ile Pro Ala Arg Arg Ser Ala Asp His Gly Ile
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 Ala Thr Asp Thr Pro Ala Thr Leu Arg Glu Arg Leu Ala Gly Leu Thr
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 Ile Pro Ala Gln Arg Thr Gly Leu Leu Leu Glu Leu Val Arg Thr His
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 Ala Ala Ala Val Leu Gly His Pro Thr Ser Ala Val Thr Ala Ala Asp
 4485 4490 4495
 Gly Ala Leu Pro Asp Asp Leu Val Pro Ala Asp Thr Glu Phe Arg Asp
 4500 4505 4510
 Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu Arg Asn Arg Ile Asn
 4515 4520 4525
 Ala Val Thr Gly Leu Arg Leu Pro Ala Thr Leu Ile Phe Asp Gln Pro
 4530 4535 4540
 Ser Pro Ala Ala Leu Ala Asp His Leu Ala Thr Arg Leu Thr Ala Glu
 4545 4550 4555 4560
 Ala Gly Thr Pro Asp Glu Pro Ala Pro Ala Ala Ala Ala Gly Ala
 4565 4570 4575
 Gly Ser Ala Gly Ser Ala Glu Thr Gly Gln Gln Arg Ser Thr Gly Ser
 4580 4585 4590
 Glu Lys Gln Gln Thr Arg Gly Gly Thr Ser Thr Glu Thr Val Glu Ser
 4595 4600 4605
 Leu Phe Trp Ile Gly His Asp Thr Arg Arg Ile Glu Glu Ser Met Ala
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 Leu Leu Ser Ala Ala Ser Phe Phe Arg Pro Ala Phe Thr Asp Pro Ser
 4625 4630 4635 4640
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 Ala Gln Gly Glu Ala Leu Ala Arg Gly Glu Thr Arg Pro Ala Leu Ile
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 Cys Leu Pro Thr Val Ala Ala Val Ser Ser Val Tyr Gln Tyr Ser Arg
 4675 4680 4685
 Phe Ala Ala Gly Leu Asn Gly His Arg Asp Val Trp Tyr Val Pro Ala
 4690 4695 4700
 Pro Gly Phe Leu Glu Gly Glu Pro Leu Pro Ser Gly Ile Gly Ala Val
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Thr Arg Met Phe Ala Asp Ala Ile Val Arg Phe Thr Asp Gly Ala Pro
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Phe Ala Leu Ala Gly His Ser Ala Gly Gly Trp Phe Val Tyr Ala Val
4740 4745 4750

Thr Ser His Leu Glu Arg Leu Gly Val Arg Pro Glu Ala Val Val Thr
4755 4760 4765

Met Asp Ala Tyr Leu Pro Asp Asp Gly Ile Ala Pro Val Ala Ser Ala
4770 4775 4780

Leu Thr Ser Glu Ile Phe Asp Arg Val Thr Gln Phe Val Asp Val Asp
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Tyr Thr Arg Leu Val Ala Met Gly Gly Tyr Phe Arg Ile Phe Ser Gly
4805 4810 4815

Trp Ser Pro Pro Asp Ile Thr Thr Pro Ala Leu Phe Leu Arg Gly Arg
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Asp Gly Glu Gln Met Pro Pro Pro Trp Gly Val Pro His Thr Val Leu
4835 4840 4845

Asp Ile Gln Gly Asn His Phe Thr Met Leu Glu Gln Phe Ala Asp Ser
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Thr Ala Arg His Val Asp Glu Trp Leu Thr Glu Ile Ala Ser Val Arg
4865 4870 4875 4880

Arg

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<211> 5532
<212> PRT
<213> Streptomyces avermitilis

<400> 6
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Lys Ala Asn Gln Thr Leu Arg Ala Arg Asn Glu Gln Leu Ala Ala Ala
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Met Glu Ala Ser Ser Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg
35 40 45

Phe Pro Gly Gly Val Cys Ser Pro Glu Glu Leu Trp Glu Leu Val Ala
50 55 60

Ser Gly Gly Asp Ala Ile Gly Glu Phe Pro Ala Gly Arg Gly Trp Asp
65 70 75 80

Leu Glu Gly Leu Phe Asp Ser Asp Pro Asp Arg Ser Gly Thr Ser Tyr
85 90 95

Ala Arg Tyr Gly Gly Phe Leu Tyr Glu Ala Gly Glu Phe Asp Ala Asp
100 105 110

Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln
 115 120 125
 Arg Leu Leu Leu Glu Thr Ser Trp Glu Ala Phe Glu Arg Ala Gly Ile
 130 135 140
 Asp Pro Leu Ser Met Arg Gly Ser Arg Thr Gly Val Phe Ala Gly Val
 145 150 155 160
 Met Tyr His Asp Tyr Gly Ser Arg Leu Gly Thr Ile Pro Glu Gly Phe
 165 170 175
 Glu Gly Tyr Ile Gly Asn Gly Ser Gly Gly Ala Val Ala Ser Gly Arg
 180 185 190
 Val Ala Tyr Thr Leu Gly Leu Glu Gly Pro Ala Val Ser Val Asp Thr
 195 200 205
 Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ser Leu
 210 215 220
 Arg Ser Gly Glu Cys Thr Leu Ala Leu Ala Gly Gly Val Thr Val Met
 225 230 235 240
 Ser Thr Pro His Leu Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ser
 245 250 255
 Val Asp Gly Arg Cys Lys Ser Phe Ala Gly Gly Ala Asp Gly Thr Gly
 260 265 270
 Met Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala
 275 280 285
 Val Arg Leu Gly His Arg Val Leu Ala Val Leu Arg Gly Ser Ala Val
 290 295 300
 Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ala
 305 310 315 320
 Gln Glu Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Ser Val
 325 330 335
 Ala Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly
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 Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Arg Ala
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 Gly Asn Arg Pro Leu Trp Leu Gly Ser Val Lys Ser Asn Ile Gly His
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 Ala Gln Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala
 385 390 395 400
 Leu Arg Glu Gly Val Leu Pro Arg Thr Leu His Val Asp Glu Pro Ser
 405 410 415
 Pro Gln Val Asp Trp Ser Ala Gly Ala Val Arg Leu Leu Thr Glu Ala
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Val	Pro	Trp	Pro	Gly	Asp	Ala	Ala	Gly	Arg	Leu	Arg	Arg	Ala	Gly	Val
		435					440					445			
Ser	Ser	Phe	Gly	Val	Ser	Gly	Thr	Asn	Ala	His	Val	Ile	Leu	Glu	Glu
	450					455					460				
Ala	Pro	Ala	Ala	Gly	Gly	Cys	Val	Ala	Gly	Gly	Gly	Val	Leu	Glu	Gly
465					470					475					480
Ala	Pro	Gly	Leu	Ala	Ile	Ser	Val	Ala	Glu	Ser	Val	Ala	Ala	Pro	Val
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			500					505					510		
Pro	Val	Pro	Val	Pro	Val	Ser	Ala	Arg	Ser	Glu	Ala	Gly	Leu	Arg	Ala
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Gln	Ala	Glu	Ala	Leu	Arg	Gln	Tyr	Val	Ala	Val	Arg	Pro	Asp	Val	Ser
	530					535					540				
Leu	Ala	Asp	Val	Gly	Ala	Gly	Leu	Ala	Cys	Gly	Arg	Ala	Val	Leu	Glu
545					550					555					560
His	Arg	Ala	Val	Val	Leu	Ala	Ala	Asp	Arg	Glu	Glu	Leu	Val	Gln	Gly
				565					570					575	
Leu	Gly	Ala	Leu	Ala	Ala	Gly	Glu	Pro	Asp	Arg	Arg	Val	Thr	Thr	Gly
			580					585					590		
His	Ala	Pro	Gly	Gly	Asp	Arg	Gly	Gly	Val	Val	Phe	Val	Phe	Pro	Gly
		595					600					605			
Gln	Gly	Gly	Gln	Trp	Ala	Gly	Met	Gly	Val	Arg	Leu	Leu	Ala	Ser	Ser
	610					615					620				
Pro	Val	Phe	Ala	Arg	Arg	Met	Gln	Ala	Cys	Glu	Glu	Ala	Leu	Ala	Pro
625					630					635					640
Trp	Val	Asp	Trp	Ser	Val	Val	Asp	Ile	Leu	Arg	Arg	Asp	Ala	Gly	Asp
				645					650					655	
Ala	Val	Trp	Glu	Arg	Ala	Asp	Val	Val	Gln	Pro	Val	Leu	Phe	Ser	Val
			660					665					670		
Met	Val	Ser	Leu	Ala	Ala	Leu	Trp	Arg	Ser	Tyr	Gly	Ile	Glu	Pro	Asp
		675					680					685			
Ala	Val	Leu	Gly	His	Ser	Gln	Gly	Glu	Ile	Ala	Ala	Ala	His	Val	Cys
						695				700					
Gly	Ala	Leu	Ser	Leu	Lys	Asp	Ala	Ala	Lys	Thr	Val	Ala	Leu	Arg	Ser
705					710					715					720
Arg	Ala	Leu	Ala	Ala	Val	Arg	Gly	Arg	Gly	Gly	Met	Ala	Ser	Val	Pro
				725					730					735	
Leu	Pro	Ala	Gln	Glu	Val	Glu	Gln	Leu	Ile	Gly	Glu	Arg	Trp	Ala	Gly
			740				745						750		

Arg	Leu	Trp	Val	Ala	Ala	Val	Asn	Gly	Pro	Arg	Ser	Thr	Ala	Val	Ser	755	760	765
Gly	Asp	Ala	Glu	Ala	Val	Asp	Glu	Val	Leu	Ala	Tyr	Cys	Ala	Gly	Thr	770	775	780
Gly	Val	Arg	Ala	Arg	Arg	Ile	Pro	Val	Asp	Tyr	Ala	Ser	His	Cys	Pro	785	790	795
His	Val	Gln	Pro	Leu	Arg	Glu	Glu	Leu	Leu	Glu	Leu	Leu	Gly	Asp	Ile	805	810	815
Ser	Pro	Gln	Pro	Ser	Gly	Val	Pro	Phe	Phe	Ser	Thr	Val	Glu	Gly	Thr	820	825	830
Trp	Leu	Asp	Thr	Thr	Thr	Leu	Asp	Ala	Ala	Tyr	Trp	Tyr	Arg	Asn	Leu	835	840	845
His	Gln	Pro	Val	Arg	Phe	Ser	Asp	Ala	Val	Gln	Ala	Leu	Ala	Asp	Asp	850	855	860
Gly	His	Arg	Val	Phe	Val	Glu	Val	Ser	Pro	His	Pro	Thr	Leu	Val	Pro	865	870	875
Ala	Ile	Glu	Asp	Thr	Thr	Glu	Asp	Thr	Ala	Glu	Asp	Val	Thr	Ala	Ile	885	890	895
Gly	Ser	Leu	Arg	Arg	Gly	Asp	Asn	Asp	Thr	Arg	Arg	Phe	Leu	Thr	Ala	900	905	910
Leu	Ala	His	Thr	His	Thr	Thr	Gly	Ile	Gly	Thr	Pro	Thr	Thr	Trp	His	915	920	925
His	His	Tyr	Thr	His	His	His	Thr	His	Pro	His	Asn	His	His	Leu	Asp	930	935	940
Leu	Pro	Thr	Tyr	Pro	Phe	Gln	Arg	Gln	His	Tyr	Trp	Leu	Asp	Ala	Pro	945	950	955
Thr	Gly	Ala	Gly	Asp	Val	Ala	Ala	Ala	Gly	Leu	Glu	Pro	Ala	Glu	His	965	970	975
Pro	Leu	Leu	Ala	Ala	Thr	Val	Gln	Leu	Ala	Asp	Thr	Asp	Gly	Cys	Leu	980	985	990
Leu	Thr	Gly	Arg	Leu	Ser	Leu	Arg	Ser	His	Pro	Trp	Leu	Gly	Asp	Tyr	995	1000	1005
Glu	Val	Gly	Gly	Ala	Val	Leu	Leu	Ser	Gly	Ser	Ala	Phe	Val	Glu	Leu	1010	1015	1020
Ala	Val	Gln	Val	Gly	Glu	Arg	Val	Gly	Cys	Thr	Arg	Ile	Glu	Gln	Leu	1025	1030	1035
Thr	Val	His	Ala	Pro	Leu	Val	Val	Pro	Val	Gly	Gly	Gly	Val	Ser	Val	1045	1050	1055
Gln	Val	Gly	Val	Ala	Ala	Ala	Asp	Gly	Glu	Gly	Arg	Arg	Leu	Val	Ser	1060	1065	1070

Val Tyr Ala Arg Gly Gly Ser Ala Cys Gly Gly Gly Gly Ala Ser Gly
1075 1080 1085

Gly Val Trp Thr Cys His Ala Ser Gly Val Leu Val Glu Ala Ala Ala
1090 1095 1100

Gly Gly Gly Val Val Val Asp Gly Leu Ala Gly Val Trp Pro Pro Arg
1105 1110 1115 1120

Gly Ala Val Ala Val Asp Val Asp Gly Val Arg Asp Arg Leu Ala Gly
1125 1130 1135

Ala Gly Cys Val Leu Gly Pro Val Phe Ser Gly Leu Arg Ala Val Trp
1140 1145 1150

Arg Asp Gly Gly Asp Leu Leu Ala Glu Val Cys Leu Pro Glu Glu Ala
1155 1160 1165

Trp Gly Asp Ala Ala Gly Phe Gly Leu His Pro Ala Leu Leu Asp Gly
1170 1175 1180

Val Val Gln Pro Leu Ser Val Leu Leu Pro Gly Gly Thr Gly Phe Gly
1185 1190 1195 1200

Glu Gly Ala Gly Phe Gly Glu Gly Val Arg Val Pro Ala Val Trp Gly
1205 1210 1215

Gly Val Ser Leu His Arg Ala Gly Val Thr Gly Val Arg Val Arg Val
1220 1225 1230

Trp Ala Val Gly Arg Gly Gly Gly Arg Glu Ala Val Ser Val Val Val
1235 1240 1245

Gly Asp Glu Ala Gly Val Pro Val Ala Ser Val Asp Arg Leu Glu Leu
1250 1255 1260

Arg Pro Val Asp Met Gly Gln Leu Arg Ala Val Ser Val Ser Ala Gly
1265 1270 1275 1280

Arg Arg Gly Ser Leu Tyr Ala Val Gln Trp Ala Glu Val Gly Pro Val
1285 1290 1295

Pro Val Cys Gly Gln Ala Trp Ala Trp His Glu Asp Val Gly Glu Ser
1300 1305 1310

Gly Gly Gly Pro Val Pro Gly Val Val Val Leu Arg Cys Pro Asp Ala
1315 1320 1325

Gly Ala Gly Gly Gly Gly Gly Gly Gly Val Gly Glu Val Val Gly Gly
1330 1335 1340

Val Leu Gly Val Val Gln Gly Trp Leu Gly Leu Glu Arg Phe Ala Gly
1345 1350 1355 1360

Ser Arg Leu Val Val Val Thr Arg Gly Ala Val Val Ala Gly Gln Glu
1365 1370 1375

Asp Gly Pro Val Asp Val Val Gly Ala Ala Val Trp Gly Leu Val Arg
1380 1385 1390

Ser Ala Gln Ala Glu His Pro Asp Arg Phe Val Leu Leu Asp Leu Asp
1395 1400 1405

Thr Asp Thr Asp Thr Gly Thr Asp Leu Asp Thr Gly Ala Gly Ala Gly
1410 1415 1420

Ala Gly Ala Gly Trp Gly Val Asp Gly Gly His Val Ala Ala Val Val
1425 1430 1435 1440

Ala Cys Gly Glu Pro Gln Leu Ala Val Arg Gly Glu Arg Val Leu Ala
1445 1450 1455

Ala Arg Leu Thr Arg Leu Glu Ser Ser Val Asp Val Pro Ala Gln Arg
1460 1465 1470

Ser Gly Asp Val Ala Gly Arg Glu Val Leu Pro Trp Leu Ser Gly Gly
1475 1480 1485

Ser Val Leu Val Thr Gly Gly Thr Gly Val Leu Gly Ala Ala Val Ala
1490 1495 1500

Arg His Leu Ala Gly Val Cys Gly Val Arg Asp Leu Leu Leu Val Ser
1505 1510 1515 1520

Arg Arg Gly Pro Asp Ala Pro Gly Ala Glu Gly Leu Arg Ala Glu Leu
1525 1530 1535

Ala Ala Leu Gly Ala Glu Val Arg Ile Val Ala Cys Asp Val Gly Glu
1540 1545 1550

Arg Arg Glu Val Val Arg Leu Leu Glu Gly Val Pro Ala Gly Cys Pro
1555 1560 1565

Leu Thr Gly Val Val His Ala Ala Gly Val Leu Asp Asp Ala Thr Ile
1570 1575 1580

Ala Ser Leu Thr Pro Glu Arg Leu Gly Thr Val Phe Ala Ala Lys Val
1585 1590 1595 1600

Asp Ala Ala Leu Leu Leu Asp Glu Leu Thr Arg Gly Met Glu Leu Ser
1605 1610 1615

Ala Phe Val Leu Phe Ser Ser Ala Ala Gly Ile Leu Gly Ser Ala Gly
1620 1625 1630

Gln Gly Asn Tyr Ala Ala Ala Asn Ala Ala Leu Asp Ala Leu Ala Tyr
1635 1640 1645

Arg Arg Arg Ala Ala Gly Leu Pro Gly Val Ser Leu Ala Trp Gly Leu
1650 1655 1660

Trp Glu Glu Ala Ser Gly Met Thr Gly His Leu Ala Gly Thr Asp His
1665 1670 1675 1680

Arg Arg Ile Ile Arg Ser Gly Leu His Pro Met Ser Thr Pro Asp Ala
1685 1690 1695

Leu Ala Leu Phe Asp Ala Ala Leu Ala Leu Asp Arg Pro Val Leu Leu
1700 1705 1710

Pro Ala Asp Leu Arg Pro Ala Pro Pro Leu Pro Pro Leu Leu Gln Asp
1715 1720 1725

Leu Leu Pro Ala Thr Arg Arg Arg Thr Thr Arg Thr Thr Thr Thr Gly
1730 1735 1740

Gly Ala Asp Asn Gly Ala Gln Leu His Ala Arg Leu Ala Gly Gln Thr
1745 1750 1755 1760

His Glu Gln Gln His Thr Thr Leu Leu Ala Leu Val Arg Ser His Ile
1765 1770 1775

Ala Thr Val Leu Gly His Thr Thr Pro Asp Thr Ile Pro Pro Asp Arg
1780 1785 1790

Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu Arg
1795 1800 1805

Asn Arg Leu Ser Arg Thr Thr Gly Leu Arg Leu Pro Thr Thr Leu Ala
1810 1815 1820

Phe Asp His Pro Asn Pro Thr Thr Leu Thr His His Leu His Thr Gln
1825 1830 1835 1840

Leu Leu Gly Ser Asp Ser Thr Ala Ser Ile Pro Ala Pro Arg Ala Ala
1845 1850 1855

Ala Val Pro Ala Asp Gln Asp Glu Pro Val Ala Ile Ile Gly Met Ala
1860 1865 1870

Cys Arg Tyr Pro Gly Gly Val Thr Ser Ala Glu Glu Leu Trp Glu Leu
1875 1880 1885

Leu Ala Ser Gly Arg Asp Thr Val Gly Glu Phe Pro Thr Asp Arg Gly
1890 1895 1900

Trp Asp Leu Glu Ala Leu Phe Asp Pro Glu Pro Gly Arg Pro Gly Thr
1905 1910 1915 1920

Ser Tyr Thr Arg Cys Gly Ser Phe Leu Tyr Asp Ala Gly Glu Phe Asp
1925 1930 1935

Ala Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro
1940 1945 1950

Gln Gln Arg Leu Leu Leu Glu Ala Ser Trp Glu Ala Met Glu Gln Ala
1955 1960 1965

Gly Ile Asp Pro Thr Thr Val Arg Gly Ser Gln Thr Gly Val Phe Ala
1970 1975 1980

Gly Leu Ile Pro Gln Ala Tyr Gly Pro Arg Leu His Glu Asn Ala Ala
1985 1990 1995 2000

Ala Asp Thr Glu Gly Tyr Val Leu Thr Gly Thr Ser Gly Ser Val Ala
2005 2010 2015

Ser Gly Arg Ile Ser Tyr Thr Phe Gly Phe Glu Gly Pro Ala Val Ser
2020 2025 2030

Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys	2035	2040	2045
Gln Ala Leu Arg Ala Gly Glu Cys Ser Met Ala Leu Ala Gly Gly Val	2050	2055	2060
Thr Val Met Ser Ser Pro Gly Ala Phe Val Glu Phe Ser Arg Gln Arg	2065	2070	2075 2080
Gly Leu Ala Ala Asp Gly His Cys Lys Ala Phe Ser Ala Ala Ala Asp	2085	2090	2095
Gly Thr Gly Trp Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu	2100	2105	2110
Ser Asp Ala Arg Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly	2115	2120	2125
Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn	2130	2135	2140
Gly Pro Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly	2145	2150	2155 2160
Leu Ser Ala Gly Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr	2165	2170	2175
Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly	2180	2185	2190
Gln Asp Arg Ala Gly Glu Gly Pro Leu Trp Leu Gly Ser Val Lys Ser	2195	2200	2205
Asn Val Gly His Thr Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys	2210	2215	2220
Met Val Met Ala Leu Arg Asn Gly Leu Leu Pro Arg Thr Leu His Val	2225	2230	2235 2240
Asp Glu Pro Ser Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu	2245	2250	2255
Leu Thr Glu Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Leu Arg Arg	2260	2265	2270
Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile	2275	2280	2285
Leu Glu Glu Ala Pro Ala His Asn Ile Pro Ser Asp Thr Pro Ala Asp	2290	2295	2300
Asp Val Pro Gly Gly Pro Pro Ala Gly Glu Asp Ala Gly Ser Gly Glu	2305	2310	2315 2320
Glu Ala Ala Ala Gly Ser Pro Gly Val Trp Pro Trp Leu Val Ser Ala	2325	2330	2335
Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln Ala Leu His Ala His	2340	2345	2350

Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp Val Gly Tyr Thr Leu
 2355 2360 2365
 Ala His Ala Arg Ala Val Phe Asp His Arg Ala Thr Leu Ile Ala Ala
 2370 2375 2380
 Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala Leu Ala Ala Gly Glu
 2385 2390 2395 2400
 Pro His Pro Ala Val Ile His Ser Ser Ala Pro Gly Gly Thr Gly Thr
 2405 2410 2415
 Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys Ser Gly Gln Gly Thr
 2420 2425 2430
 Gln Arg Pro Gly Met Ala His Gly Leu Tyr His Thr His Pro Val Phe
 2435 2440 2445
 Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu Asp Pro His Leu Asp
 2450 2455 2460
 His Pro Leu Leu Pro Leu Leu Thr Gln Asp Pro Asn Thr Gln Asp Thr
 2465 2470 2475 2480
 Thr Thr Leu Glu Glu Ala Ala Ala Leu Leu Gln Gln Thr Pro Tyr Ala
 2485 2490 2495
 Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr
 2500 2505 2510
 Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly
 2515 2520 2525
 Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala
 2530 2535 2540
 Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro
 2545 2550 2555 2560
 Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His His
 2565 2570 2575
 Ile Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro
 2580 2585 2590
 Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr
 2595 2600 2605
 Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Asn
 2610 2615 2620
 His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His
 2625 2630 2635 2640
 Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile
 2645 2650 2655
 Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr
 2660 2665 2670

Gln Gln Ala Arg Asn Thr Val Asp Ile Ala Thr Thr Thr Gln Thr Leu
2675 2680 2685

His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr
2690 2695 2700

Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Thr Pro Thr Thr Thr
2705 2710 2715 2720

Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu Thr
2725 2730 2735

Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr His
2740 2745 2750

His His Asn Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr
2755 2760 2765

Pro Phe Gln His His His Tyr Trp Leu Glu Ser Thr Gln Pro Gly Ala
2770 2775 2780

Gly Asn Val Ser Ala Ala Gly Leu Asp Pro Thr Glu His Pro Leu Leu
2785 2790 2795 2800

Gly Ala Thr Leu Glu Leu Ala Glu Gly Asp Gly Cys Leu Leu Thr Gly
2805 2810 2815

Arg Leu Ser Leu Arg Thr His Pro Trp Leu Ala Gly His Ala Val Gly
2820 2825 2830

Gly Val Val Leu Leu Pro Gly Thr Ala Phe Ala Glu Leu Ala Leu His
2835 2840 2845

Ala Gly Glu Ser Val Gly Cys Asp His Val Asp Glu Leu Thr Leu His
2850 2855 2860

Thr Pro Leu Val Ile Pro Glu Val Gly Asp Val Thr Leu Gln Val Ala
2865 2870 2875 2880

Ile Ala Ala Pro Asp Glu Ser Gly Arg Arg Met Met Thr Ile His Ser
2885 2890 2895

Arg Gly Glu Gly Gly Ser Gly Gly Ala Asp Ala Ser Ala Ser Ala Trp
2900 2905 2910

Thr Arg His Ala Ala Gly Val Leu Ser Pro Ala Lys Asp Asp Asp Thr
2915 2920 2925

Ala Ser Tyr Glu Leu Leu Ala Gly Pro Trp Pro Pro Val Gly Ala Thr
2930 2935 2940

Pro Val Asp Leu Asn Thr Ala Tyr Asp Gln Met Ala Asp Ala Gly Phe
2945 2950 2955 2960

Ala Tyr Gly Leu Ala Phe Gln Gly Leu Arg Ala Ala Trp Arg Tyr Gly
2965 2970 2975

Asp Asp Ile Leu Val Glu Ala Arg Leu Pro Glu Glu Val Ser Gly Asp
2980 2985 2990

Ala Ala Ala Tyr Gly Leu His Pro Ala Leu Leu Asp Ala Ala Leu Gln
 2995 3000 3005

Gly Thr Gly Leu Leu Ser Val Ala Gly Pro Gly Thr Pro Val Val Pro
 3010 3015 3020

His Val Trp Asn Gly Leu Arg Phe Arg Thr His Gly Ala Val Ser Val
 3025 3030 3035 3040

Arg Ala Cys Leu Ser Thr Leu Gly Ala Thr Gly Ala Ala Val Cys Val
 3045 3050 3055

Arg Ile Thr Asp Asp Thr Gly Val Pro Val Ala Ser Val Asp Arg Leu
 3060 3065 3070

Glu Leu Arg Pro Val Asp Met Gly Gln Leu Arg Ala Val Ser Val Ser
 3075 3080 3085

Ala Gly Arg Arg Gly Ser Leu Tyr Ala Val Gln Trp Ala Glu Val Gly
 3090 3095 3100

Pro Val Pro Val Cys Gly Gln Ala Trp Ala Trp His Glu Asp Val Gly
 3105 3110 3115 3120

Glu Ser Gly Gly Gly Pro Val Pro Gly Val Val Val Leu Arg Cys Pro
 3125 3130 3135

Asp Ala Gly Ala Asp Gly Gly Gly Gly Gly Val Gly Glu Val Val
 3140 3145 3150

Gly Gly Val Leu Gly Val Val Gln Gly Trp Leu Gly Leu Glu Arg Phe
 3155 3160 3165

Ala Gly Ser Arg Leu Val Val Val Thr Arg Gly Ala Val Val Ala Gly
 3170 3175 3180

Pro Glu Asp Gly Pro Val Asp Val Val Gly Ala Ala Val Trp Gly Leu
 3185 3190 3195 3200

Val Arg Ser Ala Gln Ala Glu His Pro Asp Arg Phe Val Leu Leu Asp
 3205 3210 3215

Leu Asp Thr Asp Leu Asp Ser Gly Ala Asp Ala Asp Ala Gly Asn Glu
 3220 3225 3230

Ala Gly Met Gly Ser Gly Leu Asp Gly Gly Arg Val Ala Ala Val Val
 3235 3240 3245

Ala Cys Gly Glu Pro Gln Leu Ala Val Arg Gly Glu Arg Val Leu Ala
 3250 3255 3260

Ala Arg Leu Thr Arg Leu Glu Ser Pro Val Asp Val Ser Gly Arg Glu
 3265 3270 3275 3280

Val Leu Pro Trp Leu Ser Gly Gly Ser Val Leu Val Thr Gly Gly Thr
 3285 3290 3295

Gly Val Leu Gly Ala Ala Val Ala Arg His Leu Ala Gly Val Cys Gly
 3300 3305 3310

Val Arg Asp Leu Leu Leu Val Ser Arg Arg Gly Pro Asp Ala Pro Gly
 3315 3320 3325
 Ala Glu Gly Leu Arg Ala Glu Leu Ala Ala Leu Gly Ala Glu Val Arg
 3330 3335 3340
 Ile Val Ala Cys Asp Val Gly Glu Arg Arg Glu Val Val Arg Leu Leu
 3345 3350 3355 3360
 Glu Gly Val Pro Ala Gly Cys Pro Leu Thr Gly Val Val His Ala Ala
 3365 3370 3375
 Gly Val Leu Asp Asp Ala Thr Ile Ala Ser Leu Thr Pro Glu Arg Leu
 3380 3385 3390
 Gly Thr Val Phe Ala Ala Lys Val Asp Ala Ala Leu Leu Leu Asp Glu
 3395 3400 3405
 Leu Thr Arg Gly Met Glu Leu Ser Ala Phe Val Leu Phe Ser Ser Ala
 3410 3415 3420
 Ala Gly Ile Leu Gly Ser Ala Gly Gln Gly Asn Tyr Ala Ala Ala Asn
 3425 3430 3435 3440
 Ala Ala Leu Asp Ala Leu Ala Tyr Arg Arg Arg Ala Ala Gly Leu Pro
 3445 3450 3455
 Gly Val Ser Leu Ala Trp Gly Leu Trp Glu Glu Ala Ser Gly Met Thr
 3460 3465 3470
 Gly His Leu Ala Gly Thr Asp His Arg Arg Ile Ile Arg Ser Gly Leu
 3475 3480 3485
 His Pro Met Ser Thr Pro Asp Ala Leu Ala Leu Phe Asp Ala Ala Leu
 3490 3495 3500
 Ala Leu Asp Arg Pro Val Leu Leu Pro Ala Asp Leu Arg Pro Ala Pro
 3505 3510 3515 3520
 Pro Leu Pro Pro Leu Leu Gln Asp Leu Leu Pro Ala Thr Arg Arg Arg
 3525 3530 3535
 Thr Thr Arg Thr Thr Thr Thr Gly Gly Ala Asp Asn Gly Ala Gln Leu
 3540 3545 3550
 His Ala Arg Leu Ala Gly Gln Thr His Glu Gln Gln His Thr Thr Leu
 3555 3560 3565
 Leu Ala Leu Val Arg Ser His Ile Ala Thr Val Leu Gly His Asn Ala
 3570 3575 3580
 Pro Glu Met Ile Pro Val Asp Ser Ala Phe Arg Asp Leu Gly Phe Asp
 3585 3590 3595 3600
 Ser Leu Thr Ala Val Glu Leu Arg Asn Arg Leu Gly Glu Ala Thr Gly
 3605 3610 3615
 Leu Arg Leu Pro Thr Ser Leu Val Phe Asp Gln Pro Asn Ala Ala Thr
 3620 3625 3630

Leu Ala Arg His Leu Arg Arg Glu Leu Met Gly Asp Asp Ala Glu Gly
 3635 3640 3645
 Glu Thr Pro Ser Gln Val Ala Leu His Gln Val Ala Ala Asp Glu Pro
 3650 3655 3660
 Ile Ala Ile Val Gly Met Ala Cys Arg Phe Pro Gly Gly Val Cys Ser
 3665 3670 3675 3680
 Pro Glu Glu Leu Trp Glu Leu Val Ala Ser Gly Gly Asp Ala Ile Gly
 3685 3690 3695
 Glu Phe Pro Ala Gly Arg Gly Trp Asp Leu Glu Gly Leu Phe Asp Ser
 3700 3705 3710
 Asp Pro Asp Arg Ser Gly Thr Ser Tyr Ala Arg Tyr Gly Gly Phe Leu
 3715 3720 3725
 Tyr Glu Ala Gly Glu Phe Asp Ala Asp Phe Phe Gly Ile Ser Pro Arg
 3730 3735 3740
 Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Thr Ser
 3745 3750 3755 3760
 Trp Glu Ala Phe Glu Arg Ala Gly Ile Asp Pro Leu Ser Met Arg Gly
 3765 3770 3775
 Ser Arg Thr Gly Val Phe Ala Gly Val Met Tyr His Asp Tyr Ala Ala
 3780 3785 3790
 Arg Leu His His Val Pro Glu Gly Phe Glu Gly Leu Ile Ala Asn Gly
 3795 3800 3805
 Ser Ala Gly Ser Val Ala Thr Gly Arg Val Ala Tyr Ser Phe Gly Leu
 3810 3815 3820
 Glu Gly Pro Ala Val Thr Val Asp Thr Ala Cys Ser Ser Ser Leu Val
 3825 3830 3835 3840
 Ala Leu His Trp Ala Ala Gln Ala Leu Arg Ala Gly Glu Cys Ser Met
 3845 3850 3855
 Ala Leu Ala Gly Gly Val Thr Val Met Ser Ser Pro Gly Thr Phe Val
 3860 3865 3870
 Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala Asp Gly Arg Cys Lys Ala
 3875 3880 3885
 Tyr Ser Ala Ala Ala Asp Gly Thr Gly Trp Ala Glu Gly Val Gly Met
 3890 3895 3900
 Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly His Arg Val
 3905 3910 3915 3920
 Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn
 3925 3930 3935
 Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln Gln Arg Val Ile Arg Gln
 3940 3945 3950

Ala Leu Ala Asn Ala Gly Leu Thr Pro Ala Asp Val Asp Ala Val Glu
3955 3960 3965

Gly His Gly Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala
3970 3975 3980

Leu Leu Ala Ala Tyr Gly Gln His Arg Pro His His Arg Pro Leu Trp
3985 3990 3995 4000

Leu Gly Ser Leu Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala Gly
4005 4010 4015

Val Gly Gly Val Ile Lys Met Val Met Ala Leu Arg Asn Gly Leu Leu
4020 4025 4030

Pro Gln Thr Leu His Val Asp Glu Pro Thr Pro Gln Val Asp Trp Ser
4035 4040 4045

Thr Gly Ala Val Gln Leu Leu Thr Gln Pro Val Pro Trp Pro Ala Asp
4050 4055 4060

Pro Ala Gly Arg Pro Arg His Ala Gly Val Ser Ser Phe Gly Val Ser
4065 4070 4075 4080

Gly Thr Asn Ala His Val Ile Leu Glu Glu Ala Pro Ala Ala Ala Gly
4085 4090 4095

Gly Ala Ala Gly Gly Gly Val Ser Val Gly Ala Pro Asn Pro Ala Leu
4100 4105 4110

Pro Val Ala Glu Ser Glu Pro Val Pro Val Pro Val Pro Val Ser Ala
4115 4120 4125

Arg Ser Glu Ala Gly Leu Arg Ala Gln Ala Gln Ala Leu Arg Gln Tyr
4130 4135 4140

Val Ala Ala Arg Pro Asp Met Ser Pro Ala Asp Ile Gly Ala Gly Leu
4145 4150 4155 4160

Ala Arg Gly Arg Ala Val Leu Glu His Arg Ala Val Ile Leu Ala Ala
4165 4170 4175

Asp Arg Glu Glu Leu Ala Gln Ala Leu Thr Ala Leu Ala Ala Gly Glu
4180 4185 4190

Pro His Pro His Ile Thr Thr Gly His Thr Arg Gly Ser Asp Arg Gly
4195 4200 4205

Gly Val Val Phe Val Phe Pro Gly Gln Gly Gly Gln Trp Ala Gly Met
4210 4215 4220

Gly Leu Thr Leu Leu Thr Ser Ser Pro Val Phe Ala Glu His Ile Asp
4225 4230 4235 4240

Ala Cys Glu Lys Ala Leu Thr Pro Trp Val Pro Trp Ser Leu Thr Asp
4245 4250 4255

Ile Leu His Arg Asp Pro Asp Asp Pro Ala Trp Gln Gln Ala Asp Val
4260 4265 4270

Val Gln Pro Val Leu Phe Ser Ile Met Val Ser Leu Ala Ala Leu Trp
4275 4280 4285

Arg Ser Tyr Gly Ile Glu Pro Asp Ala Val Leu Gly His Ser Gln Gly
4290 4295 4300

Glu Ile Ala Ala Ala His Ile Cys Gly Ala Leu Ser Leu Lys Asp Ala
4305 4310 4315 4320

Ala Lys Thr Val Ala Leu Arg Ser Gln Ala Leu Ala Ala Val Arg Gly
4325 4330 4335

Arg Gly Ala Met Val Ser Leu Pro Leu Pro Ala Gln Asp Val Gln Gln
4340 4345 4350

Leu Ile Ser Glu Arg Trp Glu Gly Gln Leu Trp Val Ala Ala Leu Asn
4355 4360 4365

Gly Pro His Ser Thr Thr Val Ser Gly Asp Thr Thr Ala Val Glu Glu
4370 4375 4380

Leu Leu Thr His Cys Ala Asp Thr Gly Leu Arg Ala Lys Arg Ile Pro
4385 4390 4395 4400

Val Asp Tyr Ala Ser His Cys Pro His Val Gln Pro Leu His Asp Glu
4405 4410 4415

Leu Leu His Leu Leu Gly Asp Ile Thr Pro Gln Pro Ser Thr Met Pro
4420 4425 4430

Phe Phe Ser Thr Val Val Gly His Leu Val Trp Tyr Thr Thr Thr Leu
4435 4440 4445

Asp Ala Ala Tyr Trp Tyr Arg Asn Leu His Gln Pro Val Arg Phe Ser
4450 4455 4460

His Ala Ile Gln Thr Leu Thr Asp Asp Gly His Arg Pro Phe Ile Glu
4465 4470 4475 4480

Ile Ser Pro His Pro Thr Leu Val Pro Ala Ile Glu Asp Thr Thr Glu
4485 4490 4495

Asn Thr Thr Glu Asn Ile Thr Ala Thr Gly Ser Leu Arg Arg Gly Asp
4500 4505 4510

Asn Asp Thr His Arg Phe Leu Thr Ala Leu Ala His Thr His Thr Thr
4515 4520 4525

Gly Ile Arg Thr Pro Thr Thr Trp His His His Tyr Thr Gln Thr His
4530 4535 4540

Pro His Pro His Asn His His Leu Asp Leu Pro Thr Tyr Pro Phe Gln
4545 4550 4555 4560

His Gln His Tyr Trp Leu Gln Pro Pro Thr Thr Thr Thr Asp Leu Thr
4565 4570 4575

Thr Thr Gly Leu Thr Pro Thr His His Pro Leu Leu Thr Ala Thr Leu
4580 4585 4590

Thr Leu Ala Asn Asn Asn Thr Gln Leu Leu Thr Gly Arg Leu Ser Leu
 4595 4600 4605
 Arg Thr His Pro Trp Leu Thr Asp His Thr Val Val Gly Thr Thr Leu
 4610 4615 4620
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SPECIFICATION

2/prt

Avermectin Aglycon Synthase Genes

Technical Field

The present invention relates to DNAs encoding multifunctional enzyme involved in the biosynthesis of an avermectin compound which is a polyketide; polypeptides encoded by the DNAs; vectors containing the DNAs; host cells transformed with the DNAs or the vectors; and a process for producing avermectin.

Background Art

A polyketide is a group of compounds containing a number of natural substances which vary in their structures and functions. Polyketides are known to include compounds having a variety of bioactivities such as antibacterial agents, antimyotic agents, antiparasitic agents, anti-insect agents, antitumor agents, and immunosuppressant agents, and aromatic compounds which are produced by bacteria, fungi and plants.

The above-mentioned various polyketide compounds are synthesized by the same biosynthetic mechanism which is very similar to the biosynthesis of fatty acids. That is, a polyketide compound is biosynthesized by the steps of continuous condensation of lower fatty acids including acetic acids and propionic acids, and subsequent reactions such as reduction of ketone, dehydration and enoyl reduction of each carbonyl group at β position of the extended acyl group which is similar to fatty acid synthesis. These various repetitive synthetic processes of many polyketide compounds are carried out a macromolecule, multifunctional enzyme complex, which has specific active sites (domains) required for each catalytic activity. A general reaction manner of polyketide biosynthesis is outlined, for example in Ann. Rev. Gen., 24, 37 (1990), and Ann. Rev. Microbiol., 47, 875 (1993).

It has been shown that a DNA sequence encoding polyketide synthase usually encodes all the required activities for the synthesis of a polyketide backbone. The DNA sequence encoding polyketide synthase is composed of modules, that is, repeating units involving condensation steps and modification steps following condensation. Each catalytic activity is involved in specificity to a specific carboxylic acid component of each condensation step, or in a different site which specifies a modification function following a specific condensation step to be achieved. For example, International Publication WO93/13663 describes the constitution of a gene encoding polyketide synthase of *Saccharopolyspora erythaea*. This gene consists of 6 modules, each of which is responsible for one condensation step. That is, a correct sequence of acyl side chain elongation and modification of an elongating chain are determined by genetic information present in each module.

Regarding the biosynthetic mechanism of avermectin aglycon, it has been reported that like other polyketide compounds, synthesis units of avermectin aglycon are lower fatty acids, such as acetic acid and propionic acid as its components [J. Antibiot., 39, 541-549 (1986)], and as in *Saccharopolyspora erythaea*, polyketide synthase consisting of modules is present in avermectin-producing bacteria [Gene, 115, 119-125 (1992), Ann. New York Acad. of Sci., 721, 123-132 (1994)].

Japanese Published Unexamined Patent Application No. 15391/91 describes a DNA fragment involved in avermectin biosynthesis, but shows no nucleotide sequence of the DNA fragment. This publication merely assumes the presence of polyketide synthase, which is involved in the synthesis of avermectin aglycon and the presence of partial modules. Therefore, the entire structure of polyketide synthase of avermectin cannot be predicted.

Similarly, MacNeil et al have reported a domain structure of partial modules

[Ann. New York Acad. of Sci., 721, 123-132 (1994)]. However, they have not revealed the nucleotide sequence that should be evidence for polyketide synthase of avermectin.

Alteration of polyketide synthase would be a very useful breeding technique upon breeding of bacterial strains which can be used for a novel process for producing a novel avermectin useful as veterinary drugs and agricultural chemicals, and can produce a more effective avermectin derivative. Steps required to carry out such alteration include determination of the entire nucleotide sequence of a gene encoding polyketide synthase, accurate determination of a domain structure of each module based on the sequence, and introduction of a desired mutation. However, as described above, it was very difficult to carry out such improved-breeding, since the polyketide synthase gene of avermectin aglycon had not been specified and the nucleotide sequence of the gene was unknown.

The present inventors have studied approaches for producing a component different from that produced by the wild type strain by engineering DNA involved in polyketide synthesis with various methods. To apply this methodology, first we had to isolate a DNA molecule involved in the biosynthesis of a polyketide compound.

Hence, an object of the present invention is to provide a DNA encoding a multifunctional enzyme involved in biosynthesis of avermectin aglycon, and a process for producing avermectin aglycon, altered avermectin aglycon, avermectin, and altered avermectin using the DNA.

Disclosure of the Invention

The present inventors made an intensive investigation to attain the object. As a result, the inventors have succeeded in isolating DNAs encoding a multifunctional enzyme involved in biosynthesis of avermectin aglycon. The present invention has

been completed on the basis of this result.

The present invention relates to the following (1) to (43).

- (1) A DNA encoding avermectin aglycon synthase (hereinafter, also referred to as an avermectin aglycon synthase gene).

In an embodiment of the present invention, the DNA is derived from a wild-type avermectin-producing strain or a mutant strain thereof, such as one belonging to the genus *Streptomyces*, specifically *Streptomyces avermitilis*.

- (2) A DNA comprising a nucleotide sequence selected from the group consisting of nucleotide Nos. 1-11916 and 11971-30688 of SEQ ID NO: 1, and nucleotide Nos. 1-14643 and 14824-31419 of SEQ ID NO: 2; or
a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having avermectin aglycon synthase activity.

The above term "a DNA which hybridizes with this DNA under stringent conditions" refers to a DNA which is obtained by colony hybridization, plaque hybridization or Southern hybridization or the like using the DNA having a nucleotide sequence of SEQ ID NO. 1 or 2. For example, such a DNA can be identified by carrying out hybridization at 65°C in the presence of 0.7 to 1.0 mol/l sodium chloride using a filter on which DNAs derived from colonies or plaques have been immobilized, followed by washing the filter at 65°C using 0.1 to 2-fold concentrated SSC solution (1-fold concentrated SSC solution consists of 150 mmol/l sodium chloride, 15 mmol/l sodium citrate).

Hybridization can be carried out according to a method described in experimental protocols, such as Molecular Cloning, A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989 (hereinafter abbreviated as

Molecular Cloning 2nd Edition), Current Protocols in Molecular Biology, John Wiley & Sons, 1987-1997 (hereinafter abbreviated as Current Protocols in Molecular Biology), DNA Cloning 1; Core Techniques, A Practical Approach, Second Edition, Oxford University, 1995. Specific examples of the DNA which can be hybridized include a DNA having at least homology of 80% or more, preferably 95% or more with a nucleotide sequence selected from the group consisting of nucleotide Nos. 1-11916 and 11971-30688 of SEQ ID NO: 1, and nucleotide Nos. 1-14643 and 14824-31419 of SEQ ID NO: 2.

The following term "a DNA which hybridizes with this DNA (or said DNA) under stringent conditions" can also be defined in the same manner as described above.

(3) The DNA according to the above (1) or (2) wherein the DNA comprises DNAs encoding avermectin aglycon synthase domains.

(4) The DNA according to the above (3) wherein the DNA encoding avermectin aglycon synthase domains is selected from the group consisting of:

a DNA encoding a polypeptide having acyltransferase activity and acyl carrier protein activity;

a DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, β -ketoacyl-ACP reductase activity and acyl carrier protein activity;

a DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity and acyl carrier protein activity;

a DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier protein activity; and

a DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity, acyl

carrier protein activity, and thioesterase activity.

(5) The DNA according to the above (4) wherein the DNA encoding a polypeptide having acyltransferase activity and acyl carrier protein activity is a DNA comprising the nucleotide sequence of nucleotide Nos. 85-1353 of SEQ ID NO: 1; or a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity and acyl carrier protein activity.

(6) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, β -ketoacyl-ACP reductase activity, and acyl carrier protein activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-6180, 15217-19938 and 20008-24690 of SEQ ID NO: 1, and nucleotide Nos. 100-4692 and 14935-20334 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, β -ketoacyl-ACP reductase activity, and acyl carrier protein activity.

(7) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity, and acyl carrier protein activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 6256-11658 and 24781-30309 of SEQ ID NO: 1, and nucleotide Nos. 20413-25734 and 25810-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes polypeptides having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity, and acyl carrier protein activity.

(8) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier protein activity is:

a DNA comprising the nucleotide sequence of nucleotide No. 12076-15147 of SEQ ID NO: 1, or nucleotide No. 4771-7818 of SEQ ID NO: 2;

or a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier protein activity.

(9) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity, acyl carrier protein activity, and thioesterase activity is:

a DNA comprising the nucleotide sequence of nucleotide Nos. 7906-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity, acyl carrier protein activity, and thioesterase activity.

(10) The DNA according to the above (4) wherein the DNA encoding a polypeptide having acyltransferase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 85-1032, 7906-8829, 13756-14694, 16917-17862, 21658-22584, and 26413-27336 of SEQ ID NO: 1, and nucleotide Nos. 1648-2673, 6322-7344, 9676-10773, 16543-17565, 21991-23019 and 27367-28392 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity.

(11) The DNA according to the above (4) wherein the DNA encoding a polypeptide having acyl carrier protein activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1096-1353, 5935-6180, 11413-11658, 14902-15147, 19693-19938, 24445-24690 and 30064-30309 of SEQ ID NO: 1, and nucleotide Nos. 4447-4692, 7573-7818, 13378-13659, 20089-20334, 25489-25734 and 30880-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having acyl carrier protein activity.

(12) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of SEQ ID NO: 1; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity.

(13) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β -ketoacyl-ACP reductase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 5143-5676, 10609-11142, 18886-19419, 23602-24138 and 29227-29760 of SEQ ID NO: 1, and nucleotide Nos. 3634-4188, 12547-13104, 19285-19842, 24685-25242 and 30076-30633 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP reductase activity.

(14) The DNA according to the above (4) wherein the DNA encoding a

polypeptide having dehydratase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 8947-9384 and 27475-27894 of SEQ ID NO: 1, and nucleotide Nos. 10885-11289, 23149-23529 and 28516-28878 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having dehydratase activity.

(15) The DNA according to the above (4) wherein the DNA encoding a polypeptide having thioesterase activity is:

a DNA having the nucleotide sequence of nucleotide No. 13879-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having thioesterase activity.

(16) The DNA according to the above (3) or (4) wherein the DNA encoding an avermectin aglycon synthase domain is a mutated DNA encoding a polypeptide having enhanced or diminished activity of the domain.

(17) The DNA according to the above (16) wherein the DNA encoding a polypeptide having diminished activity of avermectin aglycon synthase domain is the DNA comprising a nucleotide sequence of SEQ ID NO: 7.

(18) A DNA encoding an avermectin aglycon synthase domain which comprises a nucleotide sequence selected from the group consisting of nucleotide Nos. 85-1032, 1096-1353, 1441-2742, 3148-4068, 5143-5676, 5935-6180, 6256-7545, 7906-8829, 8947-9384, 10609-11142, 11413-11658, 12076-13368, 13756-14694, 14902-15147, 15217-16506, 16917-17862, 18886-19419, 19693-19938, 20008-21297, 21658-22584, 23602-24138, 24445-24690, 24781-26079, 26413-27336, 27475-27894, 29227-29760 and 30064-30309 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 1648-2673,

3634-4188, 4447-4692, 4771-6060, 6322-7344, 7573-7818, 7906-9258, 9676-10773, 10885-11289, 12547-13104, 13378-13659, 13879-14619, 14935-16224, 16543-17565, 17689-18066, 19285-19842, 20089-20334, 20413-21705, 21991-23019, 23149-23529, 24685-25242, 25489-25734, 25810-27102, 27367-28392, 28516-28878, 30076-30633, and 30880-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having avermectin aglycon synthase domain activity.

(19) A DNA comprising the nucleotide sequence of nucleotide No. 85-1353 of SEQ ID NO: 1 ;or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity and acyl carrier protein activity.

(20) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-6180, 15217-19938 and 20008-24690 of SEQ ID NO: 1, and nucleotide Nos. 100-4692 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, β -ketoacyl-ACP reductase activity and acyl carrier protein activity.

(21) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 6256-11658 and 24781-30309 of SEQ ID NO: 1, and nucleotide Nos. 14935-20334, 20413-25734 and 25810-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity and acyl carrier protein activity.

(22) A DNA comprising the nucleotide sequence of nucleotide No. 12076-15147 of SEQ ID NO: 1, or the nucleotide sequence of nucleotide No. 4771-7818 of SEQ ID

NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier protein activity.

(23) A DNA comprising the nucleotide sequence of nucleotide No. 7906-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity, acyl carrier protein activity, and thioesterase activity.

(24) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 85-1032, 7906-8829, 13756-14694, 16917-17862, 21658-22584 and 26413-27336 of SEQ ID NO: 1, and nucleotide Nos. 1648-2673, 6322-7344, 9676-10773, 16543-17565, 21991-23019 and 27367-28392 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity.

(25) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1096-1353, 5935-6180, 11413-11658, 14902-15147, 19693-19938, 24445-24690, and 30064-30309 of SEQ ID NO: 1, and nucleotide Nos. 4447-4692, 7573-7818, 13378-13659, 20089-20334, 25489-25734 and 30880-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having acyl carrier protein activity.

(26) A DNA comprising the nucleotide sequence selected from the group

consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705, and 25810-27102 of SEQ ID NO: 1; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity.

(27) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 5143-5676, 10609-11142, 18886-19419, 23602-24138, and 29227-29760 of SEQ ID NO: 1, and nucleotide Nos. 3634-4188, 12547-13104, 19285-19842, 24685-25242 and 30076-30633 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β ketoacyl ACP reductase activity.

(28) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 8947-9384 and 27475-27894 of SEQ ID NO: 1, and nucleotide Nos. 10885-11289, 17689-18066, 23149-23529 and 28516-28878 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having dehydratase activity.

(29) A DNA comprising the nucleotide sequence of nucleotide Nos. 13879-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having thioesterase activity.

(30) A DNA comprising the nucleotide sequence shown in SEQ ID NO: 7.

(31) A polypeptide encoded by the DNA according to any one of the above (1) to

(29) .

(32) A polypeptide comprising the amino acid sequence according to any one of SEQ ID NOS: 3 to 6; or

a polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added in the amino acid sequence according to any one of SEQ ID NOS: 3 to 6, and having avermectin aglycon synthase activity.

The above "polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added, and having avermectin aglycon synthase activity" can be prepared according to site-directed mutagenesis as described in Molecular Cloning, 2nd Edition, Current Protocols in Molecular Biology, Nucleic Acids Research, 10, 6487 (1982), Proc. Natl. Acad. Sci., USA, 79, 6409 (1982), Gene, 34, 315 (1985), Nucleic Acids Research, 13, 4431 (1985), Proc. Natl. Acad. Sci USA, 82, 488 (1985) and the like. The number of amino acids which are deleted, replaced or added is not specifically limited, but is a number of amino acids which can be deleted, replaced, or added by known methods, such as the above site-directed mutagenesis, and within the range from 1 to several tens of amino acids, preferably 1 to 20, more preferably 1 to 10, and even more preferably 1 to 5 amino acids.

(33) A polypeptide comprising the amino acid sequence selected from the group consisting of amino acid Nos. 29-344, 366-451, 481-914, 1050-1356, 1715-1892, 1979-2060, 2086-2515, 2983-3128, 3537-3714 and 3805-3886 of SEQ ID NO: 3, amino acid Nos. 36-466, 596-908, 978-1059, 1083-1512, 1653-1964, 2306-2483, 2575-2656, 2680-3109, 32030-3538, 3878-4056, 4159-4240, 4271-4703, 4815-5122, 5753-5930 and 6032-6113 of SEQ ID NO: 4, amino acid Nos. 34-461, 550-891, 1212-1396, 1483-1564, 1591-2020, 2108-2448, 2525-2606, 2636-3086, 3226-3591, 3629-3763, 4183-4363, 4460-4553 and 4627-4873 of SEQ ID NO: 5, amino acid Nos. 38-467, 574-914, 956-1081, 1488-1673, 1756-1837, 1864-2294, 2390-2732, 2776-2902,

3288-3473, 3556-3637, 3663-4093, 4182-4523, 4565-4685, 5085-5270 and 5353-5434 of SEQ ID NO: 6; or

a polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added in the amino acid sequence selected above, and having avermectin aglycon synthase domain activity.

The above "polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added in the amino acid sequence selected above, and having avermectin aglycon synthase domain activity" can be obtained according to the method described in the above (32) .

(34) A recombinant vector comprising the DNA according to any one of the above (1) to (30) .

(35) A transformant which is obtained by introducing the DNA according to any one of the above (1) to (30) or the recombinant vector of the above (34) into a host cell.

(36) The transformant according to the above (35) wherein the host cell is an avermectin-producing bacterial strain.

(37) The transformant according to the above (35) or (36) wherein the host cell is *Streptomyces avermitilis* K2038 (FERM BP-2775).

(38) A process for producing avermectin aglycon synthase or an avermectin aglycon synthase domain polypeptide comprising:

culturing the transformant according to any one of the above (35) to (37) in a medium to form and accumulate the enzyme or the domain polypeptide in the culture, and recovering the enzyme or the domain polypeptide from the culture.

(39) A process for producing avermectin aglycon or an altered avermectin aglycon comprising:

culturing the transformant according to any one of the above (35) to (37) in a medium to form and accumulate the avermectin aglycon or the altered avermectin aglycon in the culture, and

recovering the avermectin aglycon or the altered avermectin aglycon from the culture.

(40) A process for producing avermectin or altered avermectin comprising:

culturing the transformant according to any one of the above (35) to (37) in a medium to form and accumulate avermectin aglycon or altered avermectin aglycon in the culture, glycosylating the avermectin aglycon or altered avermectin glycon, and recovering avermectin or altered avermectin.

(41) The method according to the above (40) wherein altered avermectin is an avermectin which has been altered from avermectin B1a to avermectin B2a.

(42) An altered avermectin obtainable by the process according to the above (40).

(43) An oligonucleotide having a sequence corresponding to 5 to 60 continuous nucleotides in the nucleotide sequence of the DNA according to the above (1) or (2); or an oligonucleotide having a sequence complementary to the oligonucleotide.

Brief Description of the Drawings

Figure 1 is a restriction enzyme map showing *Bam*HI, *Bgl*II, *Cla*I, *Eco*RI, *Kpn*I, *Mlu*I, *Pst*I, *Stu*I and *Xho*I sites of avermectin aglycon synthase genes, *ave*AI and *ave*AI, of *Streptomyces avermitilis*. Each arrow indicates the predicted transcriptional direction of each gene.

Figure 2 shows (1) the chromosomal positions of avermectin aglycon synthase genes and the domain sequences of synthase units, (2) the estimated steps of synthesizing avermectin aglycon, and (3) the structure of 6,8a-seco-6,8a-deoxy-5-oxoAvermectin aglycon synthesized with polyketide synthases, which are the gene products of avermectin aglycon synthase genes aveAI and aveAII, and the positions of lower fatty acids which are incorporated into the skeleton of the compound. In this figure, SU indicates synthase unit, ACP indicates acyl carrier protein, AT indicates an acyltransferase, DH indicates dehydratase, DH* indicates a dehydratase-like domain which is estimated to be inactive, KR indicates β -ketoacyl-ACP reductase, KR* indicates a β -ketoacyl-ACP reductase-like domain which is estimated to be active but is not reflected in the polyketide synthetic reaction, KS indicates β -ketoacyl-ACP synthase, and TE indicates thioesterase.

Detailed Description of the Invention

The present invention will be described in detail below.

The present invention relates to DNA sequences of genes encoding avermectin aglycon synthase, and a process for producing avermectin aglycon, a basic constitutional unit of avermectin. According to the present invention, it becomes possible to produce a novel avermectin-associated compound or a specific component of avermectins by modification of the DNA to make a change to the type and number of carboxylic acids to be taken in, modification reaction after condensation, or any combination thereof.

1. Preparation of the DNA of the present invention

A DNA encoding avermectin aglycon synthase (an avermectin aglycon synthase gene) can be isolated from bacteria belonging to the genus *Streptomyces*, e.g. *Streptomyces avermitilis*.

Examples of a method for isolating an avermectin aglycon synthase gene include the method described in Japanese Published Unexamined Patent Application No. 15391/91, colony hybridization described in *Molecular Cloning*, Second Edition, etc.

Specific examples include a method which comprises: ligating the partially digested chromosomal DNA of *Streptomyces avermitilis* with appropriate restriction enzyme such as *Sau3AI*, to a cosmid vector capable of replicating in *E.coli* cleaved at a unique restriction enzyme site, e.g. the vector digested with *BamHI*; transforming *E.coli* with the obtained recombinant DNA; and selecting a transformant having the avermectin aglycon synthase gene from the obtained transformant by colony hybridization.

Examples of DNAs obtained by the above method include DNAs having the nucleotide sequences shown in SEQ ID NOS: 1 and 2.

The DNA having the nucleotide sequence of SEQ ID NO: 1 or 2 was found by chance to be a DNA fragment encoding a portion of polyketide synthase, when a gene encoding avermectin B5-O-methyl transferase (aveD) was isolated (*Gene*, 206, 175-180 (1998)), and was obtained by the above method.

Modules, domains and ORFs, which are relevant to the avermectin aglycon synthase genes of the present invention, can be determined by comparing similarity with the sequences of 3 types of polyketide synthase domains of erythromycin (*Nature*, 348, 176-178 (1990), *Science*, 252, 675-679 (1991), or *Eur. J. Biochem.*, 204, 39-49 (1992)).

Figure 1 shows a restriction map of the avermectin aglycon synthase gene regions (aveAI and aveAII) of genomic DNA (~65kbp) of *Streptomyces avermitilis* together with predicted transcription units (arrow).

Polyketide compounds are natural organic compounds having a variety of structures and functions, and the common characteristics of these compounds are that their synthesis is carried out with a multifunctional enzyme called polyketide synthase.

One polyketide synthase has substrate specificity, and catalyzes the extension of a lower fatty acid constitutional unit (which is used in the form of CoA ester of dicarboxylic acid in reactions other than initial reaction), i.e., condensation to make a polyketide carbon chain, and has a catalytic activity and a controlling activity which modify a β -carbonyl group generated from such a reaction.

The condensation reaction, which is a basic reaction in the synthesis of polyketide, needs various catalytic activities including an acyl carrier protein (ACP) activity, a β -ketoacyl-ACP synthase (KS) activity and an acyltransferase (AT) activity.

In many cases, β -carbonyl groups generated by the condensation reaction are modified. However, depending on a module, some β -carbonyl groups may not be modified and may be used for the next condensation reaction.

Catalytic activities associated with the modification of a β -carbonyl group after the condensation reaction include a β -ketoacyl-ACP reductase (KR) activity, a dehydratase (DH) activity and an enoyl reductase (ER) activity. The biosynthesis of a polyketide chain is terminated by cleaving out the polyketide chain from polyketide synthase by action of thioesterase (TE) activity.

All or several of these modification activities act in each condensation process, thereby determining the structure of a final product.

The avermectin aglycon synthase genes (aveAI and aveAII) of *Streptomyces avermitilis* are characterized in that the genes have several open reading frames each of

which comprises one or more repeating units called a module, just as with other known polyketide biosynthetic genes. A module is defined as a gene fragment which encodes activities for a one-time synthesis, i.e., a one-time condensation reaction, and the subsequent various modification reactions of the β - carbonyl group. Each module encodes ACP, KS and AT associated with the condensation reaction in polyketide synthesis, and all or several of KR, DH and ER associated with the modification reaction of the β - carbonyl group. Furthermore, there is also a module which does not have any domain for a modification reaction. A polypeptide encoding such a module is referred to as synthase unit (SU).

Figure 2 shows a biosynthetic pathway of 6,8a-seco-6,8a-deoxy-5-oxo-avermectin aglycon synthesized with avermectin aglycon synthases of *Streptomyces avermitilis*.

It is clear that PKS-1 is associated with initiation reaction, since an initiation module (SUs), differing from other modules, has acyltransferase (AT) activity on the N-terminal side. It is clear that PKS-3 is associated with the final reaction of polyketide, since module 9 (SU9) has a thioesterase (TE) domain.

The determined DNA sequences comprising avermectin aglycon synthase genes derived from *Streptomyces avermitilis* are shown in SEQ ID NOS: 1 and 2. The DNA of the present invention comprises open reading frames (ORFs) encoding respective multifunctional enzymes, and these ORFs are ORFs corresponding to nucleotide Nos. 11 to 11916 and nucleotide Nos. 211971 to 30688 of SEQ ID NO: 1 and nucleotide Nos. 31 to 14643 and nucleotide Nos. 414824 to 31419 of SEQ ID NO: 2. The amino acid sequences of various peptides encoded by these sequences are shown in SEQ ID NOS: 3, 4, 5 and 6.

Each of the above DNAs comprises a module encoding a synthesis unit

having all catalytic activities necessary for a one-time carbon chain extension reaction.

These modules are represented as the following nucleotides in SEQ ID NOS: 1 and 2.

That is to say, the modules are represented in SEQ ID NO: 1 as,

Initiation Module: 85 to 1353,

Module 1: 1441 to 6180,

Module 2: 6256 to 11658,

Module 3: 12076 to 15147,

Module 4: 15217 to 19938,

Module 5: 20008 to 24690,

Module 6: 24781 to 30309, and,

are represented in SEQ ID NO: 2 as,

Module 7: 100 to 4692,

Module 8: 4771 to 7818,

Module 9: 7906 to 14619,

Module 10: 14935 to 20334,

Module 11: 20413 to 25734,

Module 12: 25810 to 31125.

The amino acid sequences of various synthase units (SU) encoded by these modules are represented as the following amino acids. That is to say, the sequences are represented in SEQ ID NO: 3 as,

Initiation SU: 29 to 451,

SU1: 481 to 2060,

SU2: 2086 to 3886;

in SEQ ID NO: 4 as,

SU3: 36 to 1059,

SU4: 1083 to 2656,

SU5: 2680 to 4240,

SU6: 4271 to 6113;

in SEQ ID NO: 5 as,

SU7: 34 to 1564,

SU8: 1591 to 2606,

SU9: 2636 to 4873; and,

in SEQ ID NO: 6 as,

SU10: 38 to 1837,

SU11: 1864 to 3637,

SU12: 3663 to 5434.

DNAs encoding Avermectin aglycon synthase domains (submodules) are represented as the following nucleotides. That is to say, the DNAs are represented in SEQ ID NO: 1 as,

in Initiation Module,

ATs: 85 to 1032,

ACPs: 1096 to 1353;

in Module 1,

KS1: 1441 to 2742,

AT1: 3148 to 4068,

KR1: 5143 to 5676,

ACP1: 5935 to 6180;

in Module 2,

KS2: 6256 to 7545,

AT2: 7906 to 8829,

DH2: 8947 to 9384,

KR2: 10609 to 11142,
ACP2: 11413 to 11658;

in Module 3,
KS3: 12076 to 13368,
AT3: 13756 to 14694,
ACP3: 14902 to 15147;

in Module 4,
KS4: 15217 to 16506,
AT4: 16917 to 17862,
KR4: 18886 to 19419,
ACP4: 19693 to 19938;

in Module 5,
KS5: 20008 to 21297,
AT5: 21658 to 22584,
KR5: 23602 to 24138,
ACP5: 24445 to 24690;

in Module 6,
KS6: 24781 to 26079,
AT6: 26413 to 27336,
DH6: 27475 to 27894,
KR6: 29227 to 29760,
ACP6: 30064 to 30309; and,

are also represented in SEQ ID NO: 2 as,
in Module 7,

KS7: 100 to 1383,
 AT7: 1648 to 2673,
 KR7: 3634 to 4188,
 ACP7: 4447 to 4692;

in Module 8,
 KS8: 4771 to 6060,
 AT8: 6322 to 7344,
 ACP8: 7573 to 7818;

in Module 9,
 KS9: 7906 to 9258,
 AT9: 9676 to 10773,
 DH9: 10885 to 11289,
 KR9: 12547 to 13104,
 ACP9: 13378 to 13659,
 TE9: 13879 to 14619;

in Module 10,
 KS10: 14935 to 16224,
 AT10: 16543 to 17565,
 DH10: 17689 to 18066,
 KR10: 19285 to 19842,
 ACP10: 20089 to 20334;

in Module 11,
 KS11: 20413 to 21705,
 AT11: 21991 to 23019,
 DH11: 23149 to 23529,

KR11: 24685 to 25242,
ACP11: 25489 to 25734;

in Module 12,

KS12: 25810 to 27102,
AT12: 27367 to 28392,
DH12: 28516 to 28878,
KR12: 30076 to 30633,
ACP12: 30880 to 31125.

The deduced amino acid sequences of various domains encoded by these submodules are represented as:

in SEQ ID NO: 3,

ATs: 29 to 344,
ACPs: 366 to 451,
KS1: 481 to 914,
AT1: 1050 to 1356,
KR1: 1715 to 1892,
ACP1: 1979 to 2060,
KS2: 2086 to 2515,
DH2: 2983 to 3128,
KR2: 3537 to 3714,
ACP2: 3805 to 3886;

in SEQ ID NO: 4,

KS3: 36 to 466,
AT3: 596 to 908,
ACP3: 978 to 1059,
KS4: 1083 to 1512,

AT4: 1653 to 1964,
KR4: 2306 to 2483,
ACP4: 2575 to 2656,
KS5: 2680 to 3109,
AT5: 32030 to 3538,
KR5: 3878 to 4056,
ACP5: 4159 to 4240,
KS6: 4271 to 4703,
AT6: 4815 to 5122,
DH6: 5753 to 5930,
ACP6: 6032 to 6113;

in SEQ ID NO: 5,
KS7: 34 to 461,
AT7: 550 to 891,
KR7: 1212 to 1396,
ACP7: 1483 to 1564,
KS8: 1591 to 2020,
AT8: 2108 to 2448,
ACP8: 2525 to 2606,
KS9: 2636 to 3086,
AT9: 3226 to 3591,
DH9: 3629 to 3763,
KR9: 4183 to 4363,
ACP9: 4460 to 4553,
TE9: 4627 to 4873; and,

in SEQ ID NO: 6,
KS10: 38 to 467,

AT10: 574 to 914,
DH10: 956 to 1081,
KR10: 1488 to 1673,
ACP10: 1756 to 1837,
KS11: 1864 to 2294,
AT11: 2390 to 2732,
DH11: 2776 to 2902,
KR11: 3288 to 3473,
ACP11: 3556 to 3637,
KS12: 3663 to 4093,
AT12: 4182 to 4523,
DH12: 4565 to 4685,
KR12: 5085 to 5270,
ACP12: 5353 to 5434.

From a comparison of sequence information regarding the known polyketide synthase genes, it was found that a similarity of sequences exists between domains having identical functions. By using such similarity, it becomes possible to predict the domain of a novel polyketide synthase gene.

In other words, based on the above module, domain and ORF information obtained from DNAs having nucleotide sequences of SEQ ID NO: 1 and 2 derived from *Streptomyces avermitilis*, modules, domains and ORFs, which are relevant to the Avermectin aglycon synthase genes of the present invention derived from other bacteria capable of producing avermectin, can be determined.

Using a DNA having the nucleotide sequence of SEQ ID NO: 1 or 2, an avermectin aglycon synthase gene can be obtained by the following method.

A DNA having the nucleotide sequence of SEQ ID NO: 1 or 2 is digested with appropriate restriction enzymes, the DNA fragment was separated and recovered by the method described in *Molecular Cloning*, Second Edition, and an oligonucleotide consisting of the DNA fragment is used as a probe or primer.

As a probe, the DNA fragment labeled with digoxigenin etc. is preferably used. The DIG labeling & detection kit, which can be purchased from Roche Diagnostic Corp., can be used for labeling with digoxigenin.

A library is prepared from bacteria producing avermectin by genome cloning or cDNA cloning described in *Molecular Cloning*, Second Edition etc.

A clone (or a colony) which is to be cross-hybridized with the probe obtained above is selected from the library, then a plasmid is extracted from the clone by the method described in *Molecular Cloning*, Second Edition, and finally an avermectin aglycon synthase gene can be obtained from the plasmid. In addition, DNAs (i.e. submodules) and modules which encode an avermectin aglycon synthase gene domain can be obtained by the same method.

Otherwise, an avermectin aglycon synthase gene, a submodule and a module can also be obtained by direct PCR amplification, using the above library and primers prepared as above.

In a case where the only partial DNA fragment encoding an avermectin aglycon synthase exists in the plasmid extracted as above, according to standard techniques, a restriction map of the plasmid is prepared by digesting the extracted plasmid with appropriate restriction enzymes such as *Bam*HI.

A restriction enzyme map of a DNA comprising the DNA encoding the entire

avermectin polyketide synthase can be prepared by finding restriction enzyme fragments which commonly exist in several clones and binding up the cloned fragments at overlapping portions, so that the DNA encoding avermectin polyketide synthase can be obtained.

The nucleotide sequence of a DNA encoding avermectin polyketide synthase can be determined by commonly applied nucleotide sequencing analysis, e.g. the dideoxy method (*Proc. Natl. Acad. Sci. USA*, 74, 5463 (1977)), or by the analysis with a DNA sequencing analyzer such as 373A DNA sequencer (Perkin Elmer Corp.).

Specifically, a DNA sequence can be determined by directly using double-stranded plasmid DNA as a template for a cycle sequence reaction, wherein oligonucleotide primers specific for various sequences are used. Alternatively, a DNA sequence can also be determined by: cleaving a DNA fragment into its small fragments; introducing the resulting fragments into bacteria phage M13 at random; preparing an overlapping library, which comprises DNA fragments deleted successively from the termini thereof, using a library or plasmid vector comprising partially overlapping fragments; and subjecting each recombinant DNA fragment to the DNA sequencing using oligonucleotide primers specific to the vector sequence. The fluorescently labeled reactant obtained by the cycle sequence reaction can be analyzed with a DNA sequencer (e.g. Model 4000L, LiCor).

Moreover, based on the nucleotide sequence of the determined DNA, a desired DNA can also be prepared by the chemical synthesis, using a DNA synthesizer (Model 8905, Perceptive BioSystems) etc.

The obtained nucleotide sequence data can be arranged, edited and analyzed using existing software, for example, GenetyxTM (Software Development).

Using the DNAs and DNA fragments of the present invention obtained by the above method, oligonucleotides such as an antisense oligonucleotide and a sense oligonucleotide, which have a portion of the DNA sequence of the present invention, or oligonucleotides comprising an RNA can be prepared according to standard techniques. Alternatively, based on the DNA sequence information obtained as above, these oligonucleotides can also be synthesized with the above-mentioned DNA synthesizer.

Examples of the thus obtained oligonucleotides include a DNA having a sequence corresponding to 5 to 60 continuous nucleotides in the nucleotide sequence of the DNA obtained by the above-mentioned method, or a DNA having a sequence complementary to this DNA. Furthermore, the oligonucleotides of the present invention also include an RNA having a sequence complementary to these DNAs.

Examples of the thus obtained oligonucleotides include a DNA having a sequence corresponding to 5 to 60 continuous nucleotides in the nucleotide sequence of SEQ ID NO: 1 or 2, or a DNA having a sequence complementary to this DNA. Where the oligonucleotides are used as sense and antisense primers, from among the above oligonucleotides, it is preferable to apply oligonucleotides wherein melting temperature (T_m) and the number of bases do not significantly differ between both oligonucleotides.

Examples of the thus obtained oligonucleotides include ones having the nucleotide sequences shown in SEQ ID NOS: 9 to 14.

Moreover, the derivatives of these oligonucleotides (hereinafter, also referred to as oligonucleotide derivatives) can also be used as the oligonucleotides of the present invention.

Examples of the oligonucleotide derivatives include: an oligonucleotide derivative obtained by conversion of a phosphodiester phosphate bond into a

phosphorothioate bond in the above-described oligonucleotide; an oligonucleotide derivative obtained by conversion of a phosphodiester bond into a N3'-P5' phosphoamidate bond in the above-described oligonucleotide; an oligonucleotide derivative obtained by conversion of a ribose and a phosphodiester phosphate bond into a peptide nucleic acid bond in the above-described oligonucleotide; an oligonucleotide derivative obtained by substitution of uracil by C-5 propynyl uracil in the above-described oligonucleotide; an oligonucleotide derivative obtained by substitution of uracil by C-5 thiazole uracil in the above-described oligonucleotide; an oligonucleotide derivative obtained by substitution of cytosine by C-5 propynyl cytosine in the above-described oligonucleotide; an oligonucleotide derivative obtained by substitution of cytosine by phenoxazine-modified cytosine in the above-described oligonucleotide; an oligonucleotide derivative obtained by substitution of ribose by 2'-O-propyl ribose in the above-described oligonucleotide; and an oligonucleotide derivative obtained by substitution of ribose by 2'-methoxyethoxy ribose in the above-described oligonucleotide etc. (*Cell Engineering (Saibo Kogaku)* 16, 1463 (1997)).

2. Preparation of the polypeptide of the present invention

The polypeptide of the present invention can be produced by using a method described in Molecular Cloning, Second Edition or Current Protocols in Molecular Biology. For example, it can be produced by expressing the DNA of the present invention obtained as described in the above Section 1 in a host cell, according to the following procedure.

Based on the DNA of the present invention, a DNA fragment of an appropriate length containing a region encoding the polypeptide of the present invention can be prepared, if necessary. Further, DNA useful for improving the production efficiency of the polypeptide can be prepared by replacing a nucleotide in the nucleotide sequence of the region encoding the polypeptide so as to make a codon most suitable for expression

in a host cell.

The DNA fragment is inserted at a site downstream of a promoter in an appropriate expression vector to construct a recombinant vector.

The recombinant vector is introduced into a host cell suitable for the expression vector, whereby a transformant producing the polypeptide of the present invention can be obtained.

As a host cell, any bacterial cells, yeast cells, animal cells, insect cells, plant cells etc, that are capable of expressing the desired gene can be used.

As an expression vector, it is possible to use any vector that can autonomously replicate in the above host cells or can be integrated into chromosomes thereof and that contains a promoter at a position appropriate for the transcription of the DNA of the present invention.

When a prokaryote (e.g., a bacterial cell) is used as a host cell, a preferred expression vector for the polypeptide of the present invention may be a recombinant DNA construct that is autonomously replicative in prokaryotes and that comprises a promoter, a ribosome-binding sequence, the DNA of the present invention and a terminator. The vector may further comprise a gene regulating the promoter.

Examples of expression vectors include pBTrp2, pBTac1, pBTac2 (each of which is manufactured by Boehringer Mannheim), pKK233-2 (manufactured by Pharmacia), pGEX (manufactured by Pharmacia), pSE280 (manufactured by Invitrogen), pGEMEX-1 (manufactured by Promega), pQE-8 (manufactured by QIAGEN), pQE-9 (manufactured by QIAGEN), pQE-70 (manufactured by QIAGEN), pQE-60 (manufactured by QIAGEN), pET-3 (manufactured by Novagen), pET-11a

(manufactured by Novagen), pKYP10 (Japanese Published Unexamined Patent Application No. 110600/83), pKYP200 [Agric. Biol. Chem., 48, 669 (1984)], pLSA1 [Agric. Biol. Chem., 53, 277 (1989)], pGEL1 [Proc. Natl. Acad. Sci., USA, 82, 4306 (1985)], pBluescript II SK+ (manufactured by Stratagene), pBluescript II SK(-) (manufactured by Stratagene), pTrS30 [prepared from *E. coli* JM109/pTrS30 (FERM BP-5407)], pTrS32 [prepared from *E. coli* JM109/pTrS32 (FERM BP-5408)], pUC19 [Gene, 33, 103 (1985)], pSTV28 (manufactured by Takara Shuzo Co., Ltd.), pUC118 (manufactured by Takara Shuzo Co., Ltd.), pPA1 (Japanese Published Unexamined Patent Application No. 233798/88), pKC30 (Rosenberg et al., 1983, in "Methods in Enzymology," Vol. 101, pp. 123-138, Academic Press, San Diego), pKK223-3 (manufactured by Pharmacia), pDR540 (manufactured by Pharmacia), pRIT2T (manufactured by Pharmacia), and ptrc99a [Gene, 69, 301 (1988)].

As a promoter, any promoter capable of expressing in host cells, such as *E. coli*, can be used, including promoters derived from *E. coli* or a phage such as *trp* promoter (*P_{trp}*), *lac* promoter (*P_{lac}*), *P_L* promoter, *P_R* promoter and *P_{SE}* promoter, SPO1 promoter, SPO2 promoter, and penP promoter. An artificially designed, modified promoter may also be used, including a promoter obtained by binding two *P_{trp}* promoters in tandem (*P_{trp}* × 2), *tac* promoter, lac T7 promoter, and let I promoter.

It is preferable to use a plasmid having an appropriate distance (e.g., 6-18 bases) between Shine-Dalgarno sequence (i.e., ribosome-binding sequence) and an initiation codon.

A terminator is not necessarily required for expression of the recombinant DNA construct of the present invention, but it is desirably located immediately downstream of a structural gene.

A prokaryote includes a microorganism belonging to *Escherichia*, *Serratia*,

Bacillus, *Brevibacterium*, *Corynebacterium*, *Microbacterium*, *Pseudomonas*, and the like. Specific examples include *Escherichia coli* XL1-Blue, *Escherichia coli* XL2-Blue, *Escherichia coli* DH1, *Escherichia coli* MC1000, *Escherichia coli* KY3276, *Escherichia coli* W1485, *Escherichia coli* JM109, *Escherichia coli* HB101, *Escherichia coli* No.49, *Escherichia coli* W3110, *Escherichia coli* NY49, *Serratia ficaria*, *Serratia fonticola*, *Serratia liquefaciens*, *Serratia marcescens*, *Bacillus subtilis*, *Bacillus amyloliquefaciens*, *Brevibacterium ammoniagenes*, *Brevibacterium immariophilum* ATCC14068, *Brevibacterium saccharolyticum* ATCC14066, *Corynebacterium glutamicum* ATCC13032, *Corynebacterium glutamicum* ATCC14067, *Corynebacterium glutamicum* ATCC13869, *Corynebacterium acetoacidophilum* ATCC13870, *Microbacterium ammoniaphilum* ATCC15354, and *Pseudomonas* sp. D-0110.

Introduction of the recombinant DNA can be carried out by any method for introducing DNA into these host cells: for example, the calcium ion method [Proc. Natl. Acad. Sci. USA, 69, 2110 (1972)], the protoplast method (Japanese Published Unexamined Patent Application No. 248394/88) and electroporation [Nucleic Acids Research., 16, 6127 (1988)].

When a yeast cell is used as a host cell, an expression vector which can be used includes YEp13 (ATCC37115), YEp24 (ATCC37051), YCp50 (ATCC37419), pHS19, pHS15, pG-1, pXT1 (manufactured by Stratagene), pSG5 (manufactured by Stratagene), pSVK3 (manufactured by Pharmacia), pBPV, pMSG (manufactured by Pharmacia), and pSVL SV40 (manufactured by Pharmacia).

As a promoter, any promoter capable of expressing in yeast cells may be used, including PHO5 promoter, PGK promoter, GAP promoter, ADH promoter, GPD promoter, AOX1 promoter, gal 1 promoter, gal 10 promoter, heat shock polypeptide promoter, MF α 1 promoter, and CUP 1 promoter.

Examples of the host cell include yeast strains belonging to the genus *Saccharomyces*, *Schizosaccharomyces*, *Kluyveromyces*, *Trichosporon*, *Schwanniomyces*, *Pichia* and the like. Specific examples include *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Kluyveromyces lactis*, *Trichosporon pullulans*, *Schwanniomyces alluvius*, or *Pichia pastoris*.

Introduction of the recombinant DNA can be carried out by any method for introducing DNA into yeast cells: for example, electroporation [Methods in Enzymol., 194, 182 (1990)], the spheroplast method [Proc. Natl. Acad. Sci. USA, 81, 4889 (1984)], the lithium acetate method [J. Bacteriol., 153, 163 (1983)] and the method described in Proc. Natl. Acad. Sci. USA, 75, 1929 (1978).

When an animal cell is used as a host cell, an expression vector which can be used includes pcDNAI, pcDM8 (commercially available from Funakoshi), pAGE107 (Japanese Published Unexamined Patent Application No. 22979/91), pAS3-3 (Japanese Published Unexamined Patent Application No. 227075/90), pCDM8 [Nature, 329, 840 (1987)], pcDNAI/Amp (manufactured by Invitrogen), pREP4 (manufactured by Invitrogen), pAGE103 [J. Biochem, 101, 1307 (1987)], pAGE210, pAMo, and pAMoA.

As a promoter, any promoter capable of expressing in animal cells can be used, including a promoter for immediate early (IE) gene of Cytomegalovirus (CMV), SV40 early promoter or metallothionein promoter, retroviral promoter, heat shock promoter, and SR α promoter. An enhancer for IE gene of Human CMV may also be used together with such a promoter.

Host cells include mouse myeloma cells, rat myeloma cells, mouse hybridoma cells, human Namalwa or Namalwa KJM-1 cells, human fetal kidney cells, human leukemia cells, African green monkey kidney cells, chinese hamster CHO cells, or HBT5637 (Japanese Published Unexamined Patent Application No. 299/88).

Specific examples include SP2/O, NSO and the like for mouse myeloma cells, YB2/O and the like for rat myeloma cells, HEK293 (ATCC: CRL-1573), 293 and the like for human fetal kidney cells, BALL-1 and the like for human leukemia cells, and COS-1, COS-7 and the like for African green monkey kidney cells.

Introduction of the recombinant DNA can be carried out by any method for introducing DNA into animal cells: for example, electroporation [Cytotechnology, 3, 133 (1990)], the calcium phosphate method (Japanese Published Unexamined Patent Application No. 227075/90), the lipofection method [Proc. Natl. Acad. Sci. USA, 84, 7413 (1987)] and the method described in Virology, 52, 456 (1973).

When an insect cell is used as a host cell, a polypeptide can be expressed by a method described in Baculovirus Expression Vectors, A Laboratory Manual, W. H. Freeman and Company, New York (1992); Current Protocols in Molecular Biology; Molecular Biology, A Laboratory Manual; or Bio/Technology, 6, 47 (1988).

More specifically, a recombinant gene transfer vector and a baculovirus may be co-introduced into insect cells to obtain a recombinant virus in the supernatant from the cultured insect cells. Thereafter, insect cells may further be infected with the resulting recombinant virus to express the polypeptide.

Examples of the gene transfer vector used in the above procedure includes pVL1392, pVL1393, pBlueBacIII (commercially available from Invitrogen, respectively) and the like.

Examples of the baculovirus include Autographa californica nuclear polyhedrosis virus, which infects *Noctuidae* insects, and the like.

Examples of insect cells include *Spodoptera frugiperda* ovarian cells, *Trichoplusia ni* ovarian cells, cultured cells derived from silk worm ovary, and the like.

Specific examples are Sf9 and Sf21 (Baculovirus Expression Vectors, A Laboratory Manual) for *Spodoptera frugiperda* ovarian cells, High 5 and BTI-TN-5B1-4 (manufactured by Invitrogen) for *Trichoplusia ni* ovarian cells, *Bombyx mori* N4 for cultured cells derived from silk worm ovary, and the like.

Co-introduction of the recombinant gene transfer vector and the baculovirus into insect cells for recombinant virus production can be carried out by the calcium phosphate method (Japanese Published Unexamined Patent Application No. 227075/90) or the lipofection method [Proc. Natl. Acad. Sci. USA, 84, 7413 (1987)].

When a plant cell is used as a host cell, examples of an expression vector include Ti plasmid, tobacco mosaic virus vector, and the like.

As a promoter, any promoter capable of expressing in plant cells can be used, including cauliflower mosaic virus (CaMV) 35S promoter, rice actin 1 promoter, and the like.

Host cells include plant cells such as tobacco, potato, tomato, carrot, soy bean, Brassica, alfalfa, rice, wheat, barley, and the like.

Introduction of the recombinant vector can be carried out by any method for introducing DNA into plant cells: for example, the *Agrobacterium* method (Japanese Published Unexamined Patent Application No. 140885/84, Japanese Published Unexamined Patent Application No. 70080/85, WO94/00977), electroporation (Japanese Published Unexamined Patent Application No. 251887/85), and the particle gun method (Japanese Patent No. 2606856, Japanese Patent No. 2517813).

The gene can be either expressed directly, or expressed as a secreted polypeptide or a fusion polypeptide according to the method as described in Molecular Cloning, Second Edition. Expression in yeast, animal, insect or plant cells can provide a polypeptide with sugar or sugar chain attached thereto.

The polypeptide of the present invention can be produced by culturing the thus obtained transformant in a medium to produce and accumulate the polypeptide of the present invention in the culture, and recovering the polypeptide from the culture.

The transformant of the present invention can be cultured in a medium according to a conventional method used for culturing host cells.

A medium for culturing a transformant derived from a prokaryote host (e.g., *E. coli*) or a eukaryote host (e.g., yeast) may be a natural or synthetic medium insofar as the medium contains a carbon source, a nitrogen source, an inorganic salt etc., which can be assimilated by the organism, and enables the efficient culture of the transformant.

Any carbon source assimilated by the organisms can be used as a carbon source. Illustrative examples include carbohydrates such as glucose, fructose, sucrose, molasses containing them, starch or starch hydrolysate; organic acids such as acetic acid, propionic acid; alcohols such as ethanol, propanol, and the like.

Examples of the nitrogen source which can be used include ammonium salts of various inorganic or organic acids, such as ammonia, ammonium chloride, ammonium sulfate, ammonium acetate, and ammonium phosphate; other nitrogen-containing compounds; and peptone, meat extracts, yeast extracts, corn steep liquor, casein hydrolysate, soy bean meal, soy bean meal hydrolysate, various fermented cells and hydrolysates thereof and the like.

Inorganic salts which can be used include potassium dihydrogen phosphate, dipotassium hydrogen phosphate, magnesium phosphate, magnesium sulfate, sodium chloride, ferrous sulfate, manganese sulfate, copper sulfate, calcium carbonate, and the like.

Culture is carried out under aerobic conditions by shaking culture, submerged spinner culture under aeration, and the like. The culture temperature is preferably from 15 to 40°C, and culturing time is usually from 5 hours to 7 days. During the culture, pH is maintained at 3.0 to 9.0. The pH can be adjusted using an inorganic or organic acid, an alkaline solution, urea, calcium carbonate, ammonia and the like.

Also, if necessary, antibiotics such as ampicillin and tetracycline can be added to a medium during the culturing.

In a case where a microorganism is transformed with an expression vector containing an inducible promoter, the transformant can be cultured in a medium supplemented with an inducer, if necessary. For example, when an expression vector containing *lac* promoter is used for transformation, the transformant may be cultured in a medium supplemented with isopropyl- β -D-thiogalactopyranoside or the like; when an expression vector containing *trp* promoter is used for transformation, the transformant can be cultured in a medium supplemented with indole acrylic acid or the like.

A medium for culturing a transformant obtained using an animal cell as the host includes generally-used media such as RPMI 1640 medium [The Journal of the American Medical Association, 199, 519 (1967)], Eagle's MEM medium [Science, 122, 501 (1952)], DMEM medium [Virology, 8, 396 (1959)], 199 medium [Proceeding of the Society for the Biological Medicine, 73, 1 (1950)] as well as other media to which fetal calf serum or the like has been added to the above media and the like.

Culturing is generally carried out at pH 6 to 8, at a temperature of 25 to 40°C for a period of 1 to 7 days in the presence of 5% CO₂.

Also, if necessary, antibiotics such as kanamycin, penicillin and streptomycin may be added to a medium during the culturing.

A medium for culturing a transformant obtained using an insect cell as the host includes generally-used media such as TNM-FH medium (manufactured by PharMingen), Sf-900 II SFM medium (manufactured by Life Technologies), ExCell 400 and ExCell 405 [both being products of JRH Biosciences], Grace's Insect Medium [Nature, 195, 788 (1962)] or the like.

Culturing is generally carried out at pH 6 to 7, at a temperature of 25 to 30°C for a period of 1 to 5 days.

Also, if necessary, antibiotics such as gentamycin can be added to a medium during the culture.

The transformant obtained using a plant cell as the host can be cultured as a cell or can be allowed to differentiate into plant cell or organ before culture. Examples of the medium for culturing the transformant include a generally used medium such as Murashige and Skoog (MS) medium, White medium, or any one of these media further supplemented with a plant hormone such as auxin or cytokinin.

Culturing is carried out usually at pH 5 to 9, at a temperature of 20 to 40°C for a period of 3 to 60 days.

Also, if necessary, antibiotics such as kanamycin and hygromycin can be added

to a medium during the culturing.

As described above, the polypeptide of the present invention can be produced by culturing a microorganism-, animal cell-, or plant cell-derived transformant carrying a recombinant vector in which a DNA encoding the polypeptide of the present invention has been inserted according to a general manner to produce and accumulate the polypeptide, and then recovering the polypeptide from the culture.

A method for producing the polypeptide of the present invention includes intracellular production in host cells, extracellular secretion by host cells or production on outer membranes of host cells, and the method can be selected depending on the type of host cells to be used and/or the structure of polypeptide to be produced.

If the polypeptide of the present invention is produced in host cells or on outer membranes of host cells, the polypeptide can be efficiently secreted to extracellularly from the host cells by using the method of Paulson et al. [J. Biol. Chem., 264, 17619 (1989)], the method of Lowe et al. [Proc. Natl. Acad. Sci., USA, 86, 8227 (1989), Genes Develop., 4, 1288 (1990)] or methods as described in Japanese Published Unexamined Patent Application No. 336963/93 and PCT WO94/23021.

More specifically, the polypeptide of the present invention can be efficiently secreted from host cells by expressing it in a form with signal peptide using genetic recombination techniques, the signal peptide being added upstream of a portion containing the active site of the polypeptide of the present invention.

Furthermore, the amount of the production can be increased using a gene amplification system using a dihydrofolate reductase gene or the like according to the method described in Japanese Published Unexamined Patent Application No. 227075/90.

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Further, animal or plant cells introduced with a gene may be re-differentiated to create an animal individual carrying a transgene (transgenic non-human animal) or a plant individual carrying a transgene (transgenic plant), which may be used for producing the polypeptide of the present invention.

When the transformant is an animal or plant individual, the polypeptide may be obtained by feeding or cultivating the individual in a general manner to produce and accumulate the polypeptide, and then recovering the polypeptide from the animal or plant individual.

The methods for producing the polypeptide of the present invention using an animal individual include a method using an animal obtained by introducing a gene in accordance with known manners as described in American Journal of Clinical Nutrition, 63, 639S (1996); American Journal of Clinical Nutrition, 63, 627S (1996); and Bio/Technology, 9, 830 (1991).

In the case of an animal individual, for example, the polypeptide of the present invention may be obtained by feeding a transgenic non-human animal introduced with a DNA insert encoding the polypeptide of the present invention to produce and accumulate therein the polypeptide, and then recovering the polypeptide from the animal. The polypeptide can be produced and accumulated in the animal's milk (Japanese Published Unexamined Patent Application No. 309192/88), egg, and the like. As a promoter used for this purpose, any promoter can be used so long as it can be expressed in the animal, for example, mammary gland cell-specific promoters such as an α -casein promoter, a β -casein promoter, a β -lactoglobulin promoter and a whey acidic protein promoter being preferred.

The methods for producing the polypeptide of the present invention using a

plant individual include a method cultivating a transgenic plant obtained by introducing a gen encoding the polypeptide of the present invention to produce and accumulate therein the polypeptide in a known manner as described in Tissue Culture (Soshiki Baiyo), 20 (1994); Tissue Culture, 21 (1995); and Trends in Biotechnology, 15, 45 (1997), and then the polypeptide can be recovered from the plant.

For isolation and purification of the polypeptide produced by the transformant of the present invention, conventional methods for the isolation and purification of enzymes can be used.

For example, if the polypeptide of the present invention is expressed in a soluble form in cells, after completion of culturing, the cells are recovered by centrifugation, and suspended in an aqueous buffer and then disrupted with ultrasonic disrupter, French Press, Manton-Gaulin homogenizer, Dynomill or the like, to obtain a cell-free extract.

From the supernatant obtained by centrifuging the cell-free extract, a purified product can be obtained by the general method used for isolating and purifying an enzyme, for example, solvent extraction, salting-out using ammonium sulfate or the like, desalting, precipitation using an organic solvent, anion exchange chromatography using a resin, such as diethylaminoethyl (DEAE)-Sephacel, DIAION HPA-75 (manufactured by Mitsubishi Chemical) or the like, cation exchange chromatography using a resin, such as S-Sepharose FF (manufactured by Pharmacia) or the like, hydrophobic chromatography using a resin, such as butyl sepharose, phenyl sepharose or the like, gel filtration using a molecular sieve, affinity chromatography, chromatofocusing, or electrophoresis, such as isoelectronic focusing or the like, alone or in combination thereof.

When the protein is expressed as an inclusion body in the host cells, the cells are collected in the same manner, disrupted and centrifuged to recover the inclusion body of the protein as the precipitate fraction. Next, the inclusion body of the protein is solubilized with a protein-denaturing agent.

The solubilized protein solution is diluted with or dialyzed against a solution containing no protein-denaturing agent or such a dilute solution containing the protein-denaturing agent at a lower concentration that denaturation of the protein is not caused. Thus, the normal tertiary structure of the protein is reconstituted. After the procedure, a purified product of the protein can be obtained by a purification and isolation method similar to the above.

When the protein of the present invention or its glycosylated-derivative is secreted out of cells, the protein or its derivative can be collected from the culture supernatant.

Namely, the culture supernatant is obtained by treating the culture in a similar manner to the above-mentioned centrifugation or the like. Then, a purified product can be obtained from the supernatant using a purification and isolation method similar to the above.

Examples of the thus obtained protein include a protein comprising the amino acid sequence represented by SEQ ID NO:1.

Furthermore, a fusion protein of the protein of the present invention and other protein may be produced, and purified by affinity chromatography using a substance having affinity to the fusion protein. For example, the protein of the present

invention may be produced as a fusion protein with protein A according to the method of Lowe *et al.* (*Proc. Natl. Acad. Sci. USA*, 86: 8227 (1989); *Genes Develop.*, 4: 1288 (1990)), or the method described in Japanese Published Unexamined Patent Application No. 336963/93 or 823021/94, and purified by affinity chromatography using immunoglobulin G.

Moreover, the protein of the present invention may be produced as a fusion protein with Flag peptide, and the fusion protein can be purified by affinity chromatography using an anti-Flag antibody (*Proc. Natl. Acad. Sci., USA*, 86: 8227 (1989), *Genes Develop.*, 4: 1288 (1990)). Further purification can be carried out by affinity chromatography using the antibody against the protein *per se*.

Also, based on the information of the thus obtained protein, the protein of the present invention can be produced by the chemical synthesis method, such as Fmoc (fluorenylmethyloxycarbonyl) method, tBoc (t-butyloxycarbonyl) method, or the like. It can also be chemically synthesized using a peptide synthesizer manufactured by Advanced ChemTech, Perkin-Elmer, Pharmacia, Protein Technology Instrument, Synthecell-Vega, PerSeptive, Shimadzu Corporation, or the like.

3. Production of Avermectin aglycon or Avermectin

Avermectin aglycon can be produced by culturing the transformant prepared in the above Section 2, which carries the avermectin aglycon synthase gene or a module or submodule thereof, in a medium to produce and accumulate avermectin aglycon in the culture, and then recovering avermectin aglycon from the culture.

When a host used for preparation of a transformant can produce avermectin, avermectin aglycon or avermectin can be efficiently produced in any one of the transformants obtained by introducing the avermectin aglycon synthase gene or a

module or submodule thereof into the host. The transformant thus obtained can produce avermectin aglycon or avermectin with higher efficiency than that of the host.

When a host used for preparation of a transformant cannot produce avermectin, the avermectin aglycon synthase gene may be introduced into the host to obtain a transformant capable of producing avermectin aglycon.

In the production of avermectin or avermectin aglycon, the above transformant can be cultured according to a culture procedure as described in the above Section 2.

A known avermectin is a macrocyclic lactone having a 16-membered ring with two sugar residues attached thereto via glycosidic linkage. Avermectin aglycon can be converted into avermectin in a manner well known in the art, for example, by glycosylating avermectin aglycon as described in J. Bacteriol., 175, 2552-2563 (1993).

4. Production of modified Avermectin aglycon or Avermectin

Avermectin aglycon is formed through extension of lower-fatty acid units (used in the form of CoA ester of dicarboxylic acid in reactions other than the initial reaction) by avermectin aglycon synthase, i.e., condensation to give a polyketide carbon chain, and modification of β -carbonyl groups generated during the condensation.

As described above, the avermectin aglycon synthase gene is composed of modules, each module comprising DNA encoding avermectin aglycon synthase domains (submodule).

A submodule encodes ACP, KS and AT involved in condensation during polyketide synthesis, as well as KR, DH or ER involved in modification of β -carbonyl groups.

Accordingly, the carbon chain length of the aglycon part and the type of functional group on β -carbon in the condensation process can be altered by modifying a submodule, based on nucleotide sequence information of the Avermectin aglycon synthase gene determined in the above Section 1.

Further, selective inactivation of a submodule can result in production of a predictable novel avermectin or a particular component thereof alone.

By way of example, a strain producing avermectin B1a and B2a, *Streptomyces avermitilis* K2038, can be converted into a strain producing only avermectin B2a by replacing or converting a submodule DH2 region of the avermectin aglycon synthase gene by or into its inactivated form without dehydratase activity.

The submodule DH2 region can be replaced by or converted into its inactivated form, for example, by homologous recombination on submodule DH2 of the above strain to give the nucleotide sequence shown in SEQ ID NO: 7 in a general manner as described in Molecular Cloning, Second Edition.

The strain thus obtained, which becomes capable of producing a modified (or altered) avermectin aglycon, can be used to produce and obtain the modified avermectin aglycon or modified avermectin according to the general process for producing avermectin.

Best Modes for Carrying Out the Invention

The following examples are provided for illustrative purposes only, and are not intended to limit the scope of the invention clearly defined above.

Example 1: Determination of the nucleotide sequence of the Avermectin aglycon synthase gene of *Streptomyces avermitilis*

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A nucleotide sequence of the DNA encoding avermectin aglycon synthase derived from *Streptomyces avermitilis* K2033 (US Patent No. 5206155, FERM BP-2773) was determined as follows.

Continuous or overlapping DNA fragments within the avermectin aglycon synthase gene were subcloned from plasmids containing a fragment of the avermectin aglycon synthase genes (aveAI and aveAII) co-isolated with a gene encoding avermectin B5-O-transmethylase (aveD; Gene, 206, 175-180 (1998)). Nucleotide sequences of the inserted DNA fragments in these subclones were then determined.

More specifically, the entire nucleotide sequences of aveAI and aveAII were determined by subcloning BamHI-treated fragments of 3.4 kbp, 2.0 kbp, 0.5 kbp, 6.8 kbp, 7.0 kbp, 7.8 kbp, 3.7 kbp, 4.8 kbp, 1.3 kbp, 2.4 kbp, 0.7 kbp, 1.0 kbp, 5.4 kbp, 2.5 kbp, 1.9 kbp, 0.1 kbp, 7.0 kbp, 3.1 kbp, 4.7 kbp and 1.3 kbp found in the BamHI-restriction map of aveAI and aveAII shown in Figure 1; treating the inserted DNA fragments in these subclones with exonuclease III and S1 nuclease to prepare a series of deletion fragments; and then carrying out a cycle-sequencing reaction using fluorescently-labeled primers to determine a nucleotide sequence of each deletion fragment. The genes aveAI and aveAII had the nucleotide sequences shown in SEQ ID NO: 1 and SEQ ID NO: 2, respectively.

Example 2: Production of Avermectin B2a alone by nucleotide modification of dehydratase domain in module 2

Streptomyces avermitilis K2033 (FERM BP-2775) produces avermectin B1a and B2a.

The information of avermectin aglycon synthase genes (SEQ ID NOs: 1 and 2) derived from the avermectin-producing strain, which were obtained and sequenced in Example 1, indicated that avermectin was biosynthesized through the biosynthetic

pathway shown in Figure 2.

Avermectin B1a differs from avermectin B2a only in that avermectin B1a has a double bond between 22- and 23-positions in its aglycon part, while avermectin B2a has a single bond between 22- and 23-positions and a hydroxyl group at 23-position in its aglycon part.

The biosynthetic pathway for avermectin found above indicated that avermectin aglycon synthase domain DH of SU2 (DH2) is responsible for the formation of a double bond between 22- and 23-positions in the aglycon part of avermectin B1a and that avermectin aglycon synthase domain DH of SU10 (DH10) has no dehydratase activity.

Based on the idea that a strain producing only avermectin B2a could be obtained by converting DH2 into a domain without dehydratase activity like DH10, DH2 without dehydratase activity was prepared as follows.

The Avermectin aglycon synthase genes obtained in Example 1 had six DH domains: DH2, DH6, DH9, DH10, DH11 and DH12. Comparisons of nucleotide sequences of these domains showed that DH10 clearly differed from other DH domains in a consensus sequence common to dehydratase.

More specifically, amino acid sequences of DH2, DH6, DH9, DH11 and DH12, which were directly involved in the avermectin aglycon formation, were shown to include a consensus sequence of HXaaXaaXaaGXaaXaaXaaP (SEQ ID NO: 13) or HXaaXaaXaaGXaaXaaXaaS (SEQ ID NO: 14), wherein H, G, P, S and Xaa represent histidine, glycine, proline, serine and any amino acid, respectively; whereas the corresponding sequence of DH10 was YXaaXaaXaaGXaaXaaXaaS (SEQ ID NO: 15), wherein Y represents tyrosine, and Xaa, G and S are as defined above.

Thus, replacement of an N-terminal H (His) by Y (Tyr) was thought to provide dehydratase without its activity.

A DNA was constructed, which had a nucleotide sequence encoding the sequence for replacement of the N-terminal amino acid sequence -His-Ala- in the consensus sequence of DH2 [-His-Ala-Val-Gly-Gly-Thr-Val-Leu-Leu-Ser- (SEQ ID NO: 16), amino acids 3037-3046 in SEQ ID NO: 3] by the corresponding sequence of DH10: -Tyr-Glu- (amino acids 1008-1017 in SEQ ID NO: 6). That is, the DNA sequence of DH2 domain: 5'-CAT GCC-3' (nucleotides 9109-9114 in SEQ ID NO: 1) was replaced by the sequence: 5'-TAC GAG-3' as follows.

A DNA fragment of the aveAI region containing DH2 domain was digested with restriction enzyme *Sma*I, and the 2327 bp *Sma*I fragment corresponding to nucleotides 7869-10196 in SEQ ID NO: 1 was cloned into the *Sma*I site of vector plasmid pUC19.

Taq DNA polymerase buffer, dATP, dGTP, dCTP, dTTP and Taq DNA polymerase were added to the resulting recombinant plasmid, which was then divided into two aliquots.

To one of these two aliquots, a primer having the nucleotide sequence shown in SEQ ID NO: 9 (corresponding to nucleotides 9098-9127 in SEQ ID NO: 1) and an antisense primer having the nucleotide sequence shown in SEQ ID NO: 10 (corresponding to an antisense of nucleotides 9193-9222 in SEQ ID NO: 1) were added.

To the other aliquot, an antisense primer having the nucleotide sequence shown in SEQ ID NO: 11 (corresponding to an antisense of nucleotides 9098-9127 in SEQ ID NO: 1) and a primer having the nucleotide sequence shown in SEQ ID NO: 12

(corresponding to nucleotides 8948-8977 in SEQ ID NO: 1) were added.

After the addition, each aliquot was treated at 96 °C for 5 minutes, and the reaction was repeated for 5 to 10 cycles under the following conditions: at 98 °C for 15 seconds and 68 °C for 30 seconds per cycle.

After the reaction, exonuclease I and alkaline phosphatase were added to each aliquot, incubated at 37 °C for 15 minutes, and then treated at 80 °C for 10 minutes to inactivate both the enzymes.

After the inactivation of both the enzymes, Taq DNA polymerase buffer, dATP, dGTP, dCTP, dTTP, a primer having the nucleotide sequence of SEQ ID NO: 12 (corresponding to nucleotides 8948-8977 in SEQ ID NO: 1), an antisense primer having the nucleotide sequence of SEQ ID NO: 10 (corresponding to an antisense of nucleotides 9193-9222 in SEQ ID NO: 1) and Taq DNA polymerase were added to each reaction solution. Each reaction solution was then treated at 96 °C for 5 minutes, and the reaction was repeated for 25 cycles under the following conditions: at 98 °C for 15 seconds and 68 °C for 30 seconds per cycle.

After the reaction, exonuclease I and alkaline phosphatase were added to each reaction solution, incubated at 37 °C for 15 minutes, and then treated at 80 °C for 10 minutes to inactivate the enzymes.

After the inactivation of the enzymes, restriction enzymes *XcmI* and *BsaAI* were added to each reaction solution to obtain a *XcmI-BsaAI* treated DNA fragment.

Restriction enzymes *XcmI* and *BsaAI* were added to the recombinant plasmid prepared above, which carried the inserted 2327 bp *SmaI* fragment, to obtain a *XcmI-BsaAI* treated vector fragment. The *XcmI-BsaAI* treated vector fragment, T4

DNA ligase buffer, ATP and T4 DNA ligase were added to the *XcmI*-*Bsa*AI treated DNA fragment, and then incubated overnight at 22 °C to ligate these fragments together, thereby obtaining a plasmid carrying the inserted *XcmI*-*Bsa*AI treated DNA fragment.

After the transformation of *E. coli* cells with the plasmid, the recombinant plasmids were extracted from individual colonies, and each DNA fragment inserted into the vector was then confirmed for its nucleotide sequence, thereby selecting a clone carrying a fragment introduced with the intended nucleotide replacement.

The inserted DNA fragment was taken from the selected clone, and then carried out recombination with DH2 region on the chromosome of *Streptomyces avermitilis* K2038 by homologous recombination according to a method as described in Japanese Published Examined Patent Application No. 344605/92.

The resulting recombinant *Streptomyces avermitilis* K2210 was cultured under the conditions for general avermectin production, and then the resulting cells were extracted with methanol.

The resulting extract was analyzed using two procedures presented below.

(1) Procedure using thin-layer chromatography on silica gel

Chromatography condition: silica gel, Merck Silica Gel plate F254 (Merck Corp.)

Development solution: n-hexane/iso-propyl alcohol = 85/15

Detection: UV

(2) Procedure using high performance liquid chromatography

Chromatography condition: column, ODS-Hypersil-3 (Elmer Corp.)

Mobile phase: acetonitrile/methanol/water = 60/14/26

Flow rate: 0.6 ml/min

Detection: 246 nm

Temperature: room temperature

In both analytical procedures, only the same peak as that of avermectin B2a was observed. Further, the culture extract was purified by chromatographies on Sephadex LH-20 and silica gel to give the purified product. The purified product was analyzed by NMR and mass spectrometry, indicating that the above recombinant strain produced only avermectin B2a.

Namely, avermectin B2a alone could be produced and obtained according to the method as described above.

Industrial Applicability

The present invention can provide the DNAs encoding a multifunctional enzyme involved in the biosynthesis of avermectin compound useful as a pharmaceutical agent, a veterinary agent and a agricultural chemical; polypeptides encoded by the DNAs; vectors comprising the DNAs; a host cell transformed with the DNA or vector; and a process for producing avermectin or modified avermectin.

Sequence Listing Free Text

SEQ ID NO: 9 represents a primer based on the sequence between nucleotides 9098 and 9127 in SEQ ID NO: 1

SEQ ID NO: 10 represents an antisense primer based on the sequence between nucleotides 9193 and 9222 in SEQ ID NO: 1

SEQ ID NO: 11 represents an antisense primer based on the sequence between nucleotides 9098 and 9127 in SEQ ID NO: 1

SEQ ID NO: 12 represents a primer based on the sequence between nucleotides 8948 and 8977 in SEQ ID NO: 1

The scope of the present invention will be defined by the appended claims, and

it will be appreciated that other numerous variations and modifications may be made without departing from the spirit or scope of the invention. The above examples are therefore to be construed in all respects as illustrative and not restrictive. Further, equivalents of the claims will also fall within the scope of the present invention.

All of patents, patent applications and other publications cited in this specification and the contents as disclosed in the specification and/or drawings of Japanese Patent Application No. 046961/99, which is a priority document of the present application, are incorporated herein by reference in their entirety.

WHAT IS CLAIMED IS:

1. A DNA encoding avermectin aglycon synthase.
2. A DNA comprising a nucleotide sequence selected from the group consisting of nucleotide Nos. 1-11916 and 11971-30688 of SEQ ID NO: 1 and nucleotide Nos. 1-14643 and 14824-31419 of SEQ ID NO: 2; or
a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having avermectin aglycon synthase activity.
3. The DNA according to claim 1 or 2 wherein the DNA comprises DNAs encoding avermectin aglycon synthase domains.
4. The DNA according to claim 3 wherein the DNAs encoding avermectin aglycon synthase domains are selected from the group consisting of:
a DNA encoding a polypeptide having acyltransferase activity and acyl carrier protein activity;
a DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, β -ketoacyl-ACP reductase activity and acyl carrier protein activity;
a DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity and acyl carrier protein activity;
a DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier protein activity; and
a DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity, acyl carrier protein activity, and thioesterase activity.

5. The DNA according to claim 4 wherein the DNA encoding a polypeptide having acyltransferase activity and acyl carrier protein activity is the DNA comprising a nucleotide sequence of nucleotide Nos. 85-1353 of SEQ ID NO: 1; or a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity and acyl carrier protein activity.

6. The DNA according to claim 4 wherein the DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, β -ketoacyl-ACP reductase activity, and acyl carrier protein activity is:
a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-6180, 15217-19938 and 20008-24690 of SEQ ID NO: 1, and nucleotide Nos. 100-4692 and 14935-20334 of SEQ ID NO: 2; or
a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, β -ketoacyl-ACP reductase activity, and acyl carrier protein activity.

7. The DNA according to claim 4 wherein the DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity, and acyl carrier protein activity is:
a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 6256-11658 and 24781-30309 of SEQ ID NO: 1, and nucleotide Nos. 20413-25734 and 25810-31125 of SEQ ID NO: 2; or
a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity, and acyl carrier protein activity.

8. The DNA according to claim 4 wherein the DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier

protein activity is:

a DNA comprising the nucleotide sequence of nucleotide No. 12076-15147 of SEQ ID NO: 1, or nucleotide No. 4771-7818 of SEQ ID NO: 2;

or a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier protein activity.

9. The DNA according to claim 4 wherein the DNA encoding polypeptides having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity, acyl carrier protein activity, and thioesterase activity is:

a DNA comprising the nucleotide sequence of nucleotide Nos. 7906-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity, acyl carrier protein activity, and thioesterase activity.

10. The DNA according to claim 4 wherein the DNA encoding a polypeptide having acyltransferase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 85-1032, 7906-8829, 13756-14694, 16917-17862, 21658-22584, and 26413-27336 of SEQ ID NO: 1, and nucleotide Nos. 1648-2673, 6322-7344, 9676-10773, 16543-17565, 21991-23019 and 27367-28392 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity.

11. The DNA according to claim 4 wherein the DNA encoding a polypeptide having acyl carrier protein activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1096-1353, 5935-6180, 11413-11658, 14902-15147, 19693-19938, 24445-24690 and 30064-30309 of SEQ ID NO: 1, and nucleotide Nos. 4447-4692, 7573-7818, 13378-13659, 20089-20334, 25489-25734 and 30880-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having acyl carrier protein activity.

12. The DNA according to claim 4 wherein the DNA encoding a polypeptide having β -ketoacyl-ACP synthase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of SEQ ID NO: 1; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity.

13. The DNA according to claim 4 wherein the DNA encoding a polypeptide having β -ketoacyl-ACP reductase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 5143-5676, 10609-11142, 18886-19419, 23602-24138 and 29227-29760 of SEQ ID NO: 1, and nucleotide Nos. 3634-4188, 12547-13104, 19285-19842, 24685-25242 and 30076-30633 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP reductase activity.

14. The DNA according to claim 4 wherein the DNA encoding a polypeptide having dehydratase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of

nucleotide Nos. 8947-9384 and 27475-27894 of SEQ ID NO: 1, and nucleotide Nos. 10885-11289, 23149-23529 and 28516-28878 of SEQ ID NO: 2; or
a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having dehydratase activity.

15. The DNA according to claim 4 wherein the DNA encoding a polypeptide having thioesterase activity is:

a DNA comprising the nucleotide sequence of nucleotide No. 13879-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having thioesterase activity.

16. The DNA according to claim 3 or 4 wherein the DNA encoding avermectin aglycon synthase domains is a mutated DNA encoding a polypeptide having enhanced or diminished activity of the domain.

17. The DNA according to claim 16 wherein the DNA encoding a polypeptide having diminished activity of Avermectin aglycon synthase domain is a DNA comprising the nucleotide sequence of SEQ ID NO: 7.

18. A DNA encoding an Avermectin aglycon synthase domain which comprises a nucleotide sequence selected from the group consisting of: nucleotide Nos. 85-1032, 1096-1353, 1441-2742, 3148-4068, 5143-5676, 5935-6180, 6256-7545, 7906-8829, 8947-9384, 10609-11142, 11413-11658, 12076-13368, 13756-14694, 14902-15147, 15217-16506, 16917-17862, 18886-19419, 19693-19938, 20008-21297, 21658-22584, 23602-24138, 24445-24690, 24781-26079, 26413-27336, 27475-27894, 29227-29760 and 30064-30309 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 1648-2673, 3634-4188, 4447-4692, 4771-6060, 6322-7344, 7573-7818, 7906-9258, 9676-10773, 10885-11289, 12547-13104, 13378-13659, 13879-14619, 14935-16224, 16543-17565,

17689-18066, 19285-19842, 20089-20334, 20413-21705, 21991-23019, 23149-23529, 24685-25242, 25489-25734, 25810-27102, 27367-28392, 28516-28878, 30076-30633 and 30880-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having avermectin aglycon synthase domain activity.

19. A DNA comprising the nucleotide sequence of nucleotide No. 85-1353 of SEQ ID NO: 1 ;or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity and acyl carrier protein activity.

20. A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-6180, 15217-19938, and 20008-24690 of SEQ ID NO: 1, and nucleotide Nos. 100-4692 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, β -ketoacyl-ACP reductase activity and acyl carrier protein activity.

21. A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 6256-11658, and 24781-30309 of SEQ ID NO: 1, and nucleotide Nos. 14935-20334, 20413-25734 and 25810-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity and acyl carrier protein activity.

22. A DNA comprising the nucleotide sequence of nucleotide No. 12076-15147 of SEQ ID NO: 1, or the nucleotide sequence of nucleotide No. 4771-7818 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes

a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier protein activity.

23. A DNA comprising the nucleotide sequence of nucleotide No. 7906-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β -ketoacyl-ACP reductase activity, acyl carrier protein, and thioesterase activity.

24. A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 85-1032, 7906-8829, 13756-14694, 16917-17862, 21658-22584 and 26413-27336 of SEQ ID NO: 1, and nucleotide Nos. 1648-2673, 6322-7344, 9676-10773, 16543-17565, 21991-23019 and 27367-28392 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity.

25. A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1096-1353, 5935-6180, 11413-11658, 14902-15147, 19693-19938, 24445-24690 and 30064-30309 of SEQ ID NO: 1, and nucleotide Nos. 4447-4692, 7573-7818, 13378-13659, 20089-20334, 25489-25734 and 30880-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having acyl carrier protein activity.

26. A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297, and 24781-26079 of SEQ ID NO: 1 and nucleotide Nos. 100-1383,

4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of SEQ ID NO: 1; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP synthase activity.

27. A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 5143-5676, 10609-11142, 18886-19419, 23602-24138 and 29227-29760 of SEQ ID NO: 1, and nucleotide Nos. 3634-4188, 12547-13104, 19285-19842, 24685-25242 and 30076-30633 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β -ketoacyl-ACP reductase activity.

28. A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 8947-9384 and 27475-27894 of SEQ ID NO: 1, and nucleotide Nos. 10885-11289, 17689-18066, 23149-23529 and 28516-28878 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having dehydratase activity.

29. A DNA comprising the nucleotide sequence of nucleotide Nos. 13879-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having thioesterase activity.

30. A DNA comprising the nucleotide sequence shown in SEQ ID NO: 7.

31. A polypeptide encoded by the DNA according to any one of claims 1 to 29.

32. A polypeptide comprising an amino acid sequence according to any one of

SEQ ID NOS: 3 to 6; or

a polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added in the amino acid sequence according to any one of SEQ ID NOS: 3 to 6, and having avermectin aglycon synthase activity.

33. A polypeptide comprising the amino acid sequence selected from the group consisting of amino acid Nos. 29-344, 366-451, 481-914, 1050-1356, 1715-1892, 1979-2060, 2086-2515, 2983-3128, 3537-3714 and 3805-3886 of SEQ ID NO: 3, amino acid Nos. 36-466, 596-908, 978-1059, 1083-1512, 1653-1964, 2306-2483, 2575-2656, 2680-3109, 32030-3538, 3878-4056, 4159-4240, 4271-4703, 4815-5122, 5753-5930 and 6032-6113 of SEQ ID NO: 4, amino acid Nos. 34-461, 550-891, 1212-1396, 1483-1564, 1591-2020, 2108-2448, 2525-2606, 2636-3086, 3226-3591, 3629-3763, 4183-4363, 4460-4553 and 4627-4873 of SEQ ID NO: 5, amino acid Nos. 38-467, 574-914, 956-1081, 1488-1673, 1756-1837, 1864-2294, 2390-2732, 2776-2902, 3288-3473, 3556-3637, 3663-4093, 4182-4523, 4565-4685, 5085-5270 and 5353-5434 of SEQ ID NO: 6; or

a polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added in the amino acid sequence selected above, and having avermectin aglycon synthase domain activity.

34. A recombinant vector comprising the DNA according to any one of claims 1 to 30.

35. A transformant obtainable by introducing the DNA according to any one of claims 1 to 30 or the recombinant vector according to claim 34 into a host cell.

36. The transformant according to claim 35 wherein the host cell is an avermectin-producing bacterial strain.

37. The transformant according to claim 35 or 36 wherein the host cell is *Streptomyces avermitilis* K2038 (FERM BP-2775).

38. A process for producing avermectin aglycon synthase or avermectin aglycon synthase domain polypeptide comprising:
culturing the transformant according to any one of claims 35 to 37 in a medium to produce and accumulate the enzyme or the domain polypeptide in the culture, and recovering the enzyme or the domain polypeptide from the culture.

39. A process for producing avermectin aglycon or altered avermectin aglycon comprising:

culturing a transformant according to any one of claims 35 to 37 in a medium to produce and accumulate the avermectin aglycon or the altered avermectin aglycon in the culture, and

recovering the avermectin aglycon or the altered avermectin aglycon from the culture.

40. A process for producing avermectin or altered avermectin comprising:
culturing a transformant according to any one of claims 35 to 37 in a medium to produce and accumulate the avermectin aglycon or the altered avermectin aglycon in the culture,
glycosylating the avermectin aglycon or the altered avermectin glycon, and recovering the resulting avermectin or altered avermectin.

41. The process according to claim 40 wherein altered avermectin is avermectin which has been altered from avermectin B1a to avermectin B2a.

42. An altered avermectin obtainable by the process according to claim 40.

43. An oligonucleotide having a sequence corresponding to 5 to 60 continuous nucleotides in the nucleotide sequence of the DNA according to claim 1 or 2; or an oligonucleotide having a sequence complementary to the oligonucleotide.

ABSTRACT

The present invention relates to an isolated DNA which comprises a DNA sequence encoding avermectin aglycon synthase domains that corresponds to multifunctional enzyme proteins involved in the biosynthesis of a polyketide compound, or its mutants having avermectin aglycon synthase activity, particularly functional modules and submodules in the DNA sequence derived from *Streptomyces avermitilis*, a polypeptide or mutants thereof encoded by the DNA or the mutants, a vector containing the DNA or the mutants, a host cell transformed with the DNA, the mutants thereof, or the vector, and a method for producing avermectin.

FIG.1

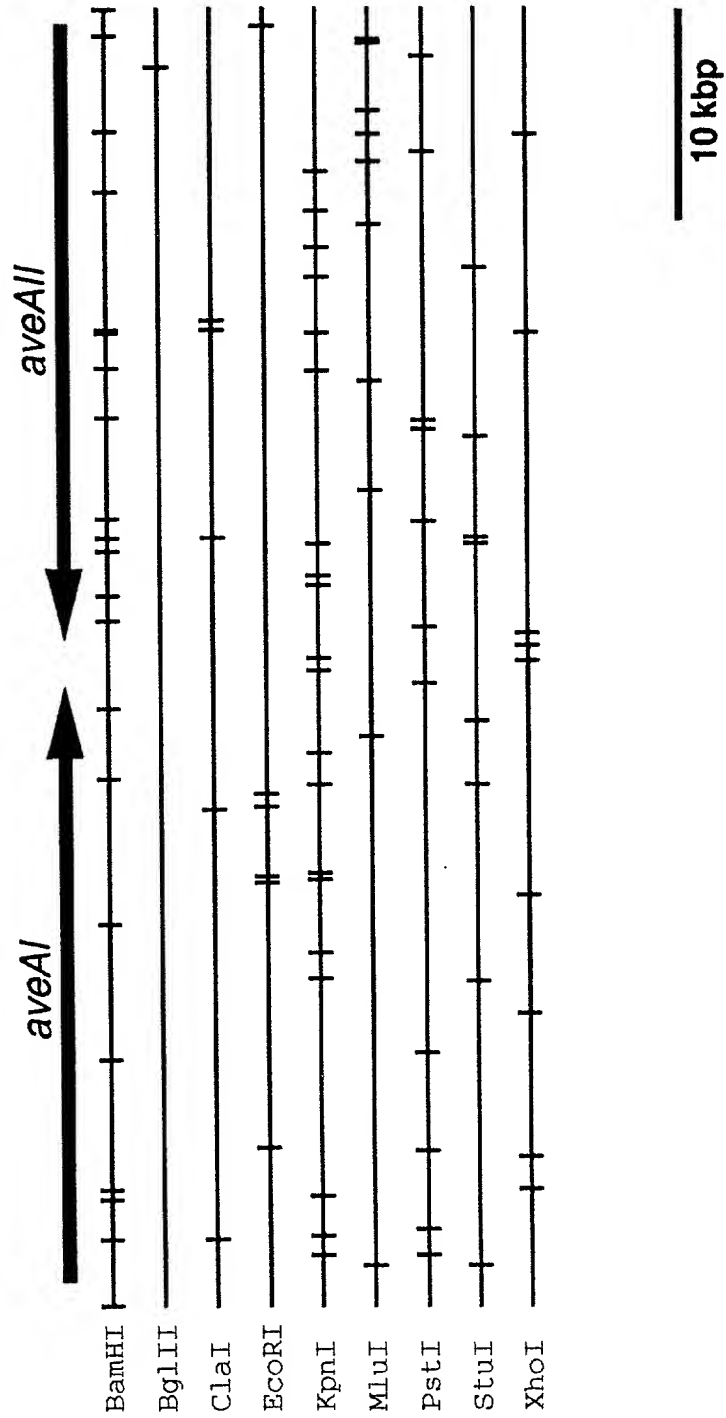
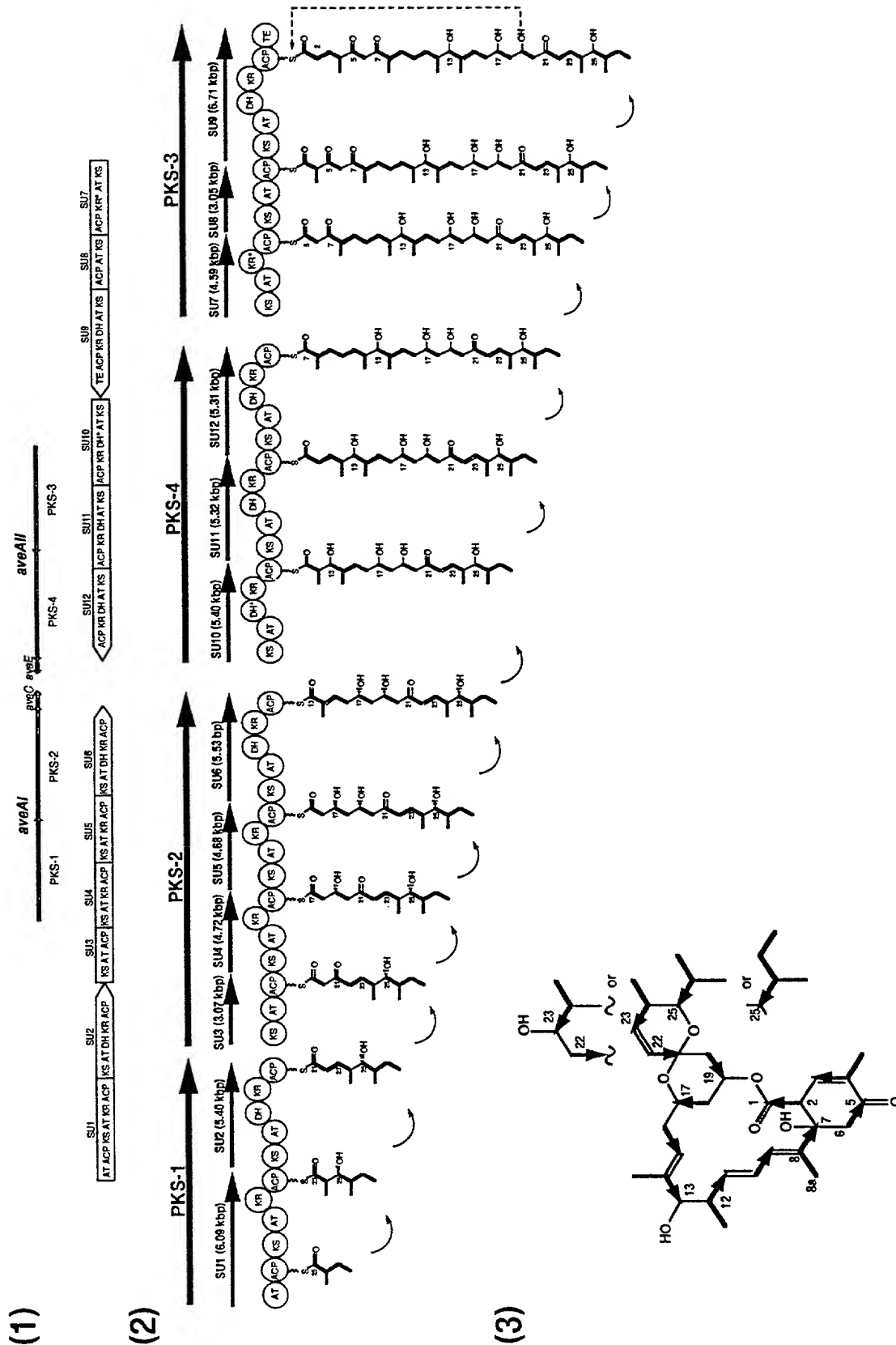


FIG.2

09/914286



Attorneys Docket No.: _____

DECLARATION, POWER OF ATTORNEY AND PETITION

I (We), the undersigned inventor(s), hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I (We) believe that I am (we are) the original, first, and joint (sole) inventor(s) of the subject matter which is claimed and for which a patent is sought on the invention entitled

AVERMECTIN AGLYCON SYNTHASE GENES

_____ the specification of which

☐ is attached hereto.

☐ was filed on _____ as

Application Serial No. _____

and amended on _____.

☒ was filed as PCT international application

Number PCT/JP00/01041

on February 23, 2000,

and was amended under PCT Article 19

on _____ (if applicable).

I (We) hereby state that I (We) have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above; that I (We) do not know and do not believe that this invention was ever known or used before my invention or discovery thereof, or patented or described in any printed publication in any country before my invention or discovery thereof, or more than one year prior to this application, or in public use or on sale in the United States for more than one year prior to this application; that this invention or discovery has not been patented or made the subject of an inventor's certificate in any country foreign to the United States on an application filed by me or my legal representatives or assigns more than twelve months before this application.

Variable	Mean		SD		t		p	
	Control	Case	Control	Case	Control	Case	Control	Case
Age	30.5	30.5	1.2	1.2	0.0	0.0	0.999	0.999
Gender	15	15	0	0	0.0	0.0	0.999	0.999
Education	12.5	12.5	1.0	1.0	0.0	0.0	0.999	0.999
Occupation	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Marital status	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Religion	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Income	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Health status	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family size	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Urban/rural	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Marital satisfaction	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Parental satisfaction	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Child satisfaction	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family cohesion	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family conflict	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family communication	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family support	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family stability	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family well-being	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family happiness	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family love	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family respect	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family trust	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family cooperation	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family harmony	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family peace	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family joy	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family hope	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family faith	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family courage	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family wisdom	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family strength	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family resilience	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family adaptability	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family flexibility	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family openness	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family inclusiveness	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family acceptance	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family tolerance	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family compassion	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family empathy	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family understanding	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family patience	1.5	1.5	0.5	0.5	0.0	0.0	0.999	0.999
Family kindness	1.5	1.5	0.5	0.5				

Application No.	Country	Filing date	Priority claimed	
<u>46961/1999</u>	<u>Japan</u>	<u>February 24, 1999</u>	<input checked="" type="checkbox"/> Yes	<input type="checkbox"/> No
<u> </u>	<u> </u>	<u> </u>	<input type="checkbox"/> Yes	<input type="checkbox"/> No
<u> </u>	<u> </u>	<u> </u>	<input type="checkbox"/> Yes	<input type="checkbox"/> No
<u> </u>	<u> </u>	<u> </u>	<input type="checkbox"/> Yes	<input type="checkbox"/> No

(Application Number)

(Filing Date)

(Application Number)

(Filing Date)

I (We) hereby claim the benefit under Section 120 of Title 35 United States Code, of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Section 112 of Title 35 United States Code, I (We) acknowledge the duty to disclose material information as defined in Section 1.56(a) of Title 37 Code of Federal Regulations, which occurred between the filing date of the prior application and national or PCT international filing date of this application:

Application Serial No.	Filing Date	Status (pending, patented, abandoned)
_____	_____	_____
_____	_____	_____
_____	_____	_____

And I (We) hereby appoint: Arthur R. Crawford (Reg. No. 25,327), Larry S. Nixon (Reg. No. 25,640), Robert A. Vanderhye (Reg. No. 27,076), James T. Hosmer (Reg. No. 30,184), Robert W. Faris (Reg. No. 31,352), Richard G. Besha (Reg. No. 22,770), Mark E. Nusbaum (Reg. No. 32,348), Michael J. Keenan (Reg. No. 32,106), Bryan H. Davidson (Reg. No. 30,251), Stanley C. Spooner (Reg. No. 27,393), Leonard C. Mitchard (Reg. No. 29,009), Duane M. Byers (Reg. No. 33,363), Paul J. Henon (Reg. No. 33,626), Jeffry H. Nelson (Reg. No. 30,481), John R. Lastova (Reg. No. 33,149), H. Warren Burnam, Jr. (Reg. No. 29,366), Thomas E. Byrne (Reg. No. 32,205), Mary J. Wilson (Reg. No. 32,955), J. Scott Davidson (Reg. No. 33,489), Alan M. Kagen (Reg. No. 36,178), William J. Griffin (Reg. No. 31,260), Robert A. Molan (Reg. No. 29,834), B. J. Sadoff (Reg. No. 36,663) and James D. Berquist (Reg. No. 34,776).

I(We) hereby request that all correspondence regarding this application be sent to the firm of NIXON & VANDERHYE P. C. whose Post office address is: 1100 North Glebe Rd., 8th Floor, Arlington, VA 22201-4714 U.S.A.

I (We) declare further that all statements made herein of my (our) knowledge are true and that all statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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Satoshi Omura
 Signature of Inventor

Citizen of: Japan

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24 09914286 082401

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Haruo IKEDA

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August 6, 2001

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09914285 09249
T01230 5824T550

配列表

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<151> 24-FEB-1999

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ttc ttc ggc atc agc ccc cgc gaa gcc ctc gcc atg gac ccc cag caa 6528
Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln
2165 2170 2175

cga ctc ctc ctc gaa acc gcc tgg gaa acc atc gaa cac gcc ggc atc 6576
Arg Leu Leu Leu Glu Thr Ala Trp Glu Thr Ile Glu His Ala Gly Ile
2180 2185 2190

aac ccc cac acc ctc cac ggc acc ccc acc gga gtc ttc acc ggc acc 6624
Asn Pro His Thr Leu His Gly Thr Pro Thr Gly Val Phe Thr Gly Thr
2195 2200 2205

aac gga cag gac tac gca ctt cgc gtg cac aac gcg ggc cag tca acc 6672
Asn Gly Gln Asp Tyr Ala Leu Arg Val His Asn Ala Gly Gln Ser Thr
2210 2215 2220

gat ggt ttc gca ctg acc gga acc gcc ggc agc gtc atc tcc ggt cgt 6720
Asp Gly Phe Ala Leu Thr Gly Thr Ala Gly Ser Val Ile Ser Gly Arg
2225 2230 2235 2240

atc tcg tac acg ttt ggt ttt gag ggt cct gcg gtg tcg gtg gac acg 6768
Ile Ser Tyr Thr Phe Gly Phe Glu Gly Pro Ala Val Ser Val Asp Thr
2245 2250 2255

gct tgt tcc tcg tcg ttg gtg gct ttg cat ctg gcc tgt cag gcg ttg 6816
Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala Leu
2260 2265 2270

cgt gcg ggt gag tgc tcg atg gcg ctt gcc ggg ggt gtg acg gtg atg 6864
Arg Ala Gly Glu Cys Ser Met Ala Leu Ala Gly Gly Val Thr Val Met
2275 2280 2285

tcg tct ccg ggt gcc ttc gtg gag ttt tcg cgg cag cgg ggt ctg gcc 6912
Ser Ser Pro Gly Ala Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala
2290 2295 2300

gcg gac ggg cat tgc aag gcg ttc tcg gcg gcg gcg gac ggg acc ggc	6960
Ala Asp Gly His Cys Lys Ala Phe Ser Ala Ala Ala Asp Gly Thr Gly	
2305 2310 2315 2320	
tggt ggt gag ggt gtg ggg atg ctg ctg gtg gag cgg ctc tcc gac gcc	7008
Trp Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala	
2325 2330 2335	
cat cgc aac ggt cac cgt gtc ctg gcc gtg gtg cgt ggc agt gcg gtc	7056
His Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val	
2340 2345 2350	
aac cag gac ggt gcg agc aac ggt ctg acc gcg ccc aac ggg ccg tcc	7104
Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser	
2355 2360 2365	
cag cag cgt gtc atc cgc cag gcc ctc gcc aac gcc ggc ttg tcg gcc	7152
Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Ser Ala	
2370 2375 2380	
ggt gat gtc gac gcg gtg gag gcc cac ggc acc ggc acc act ttg ggc	7200
Gly Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Thr Leu Gly	
2385 2390 2395 2400	
gac ccg atc gag gcc cag gcc ctc ctc gcg acc tac gga cag gac cgt	7248
Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Asp Arg	
2405 2410 2415	
gcc ggc gag ggg ccg ctg tgg ctg ggc tcg gtc aag tcc aat gtc ggt	7296
Ala Gly Glu Gly Pro Leu Trp Leu Gly Ser Val Lys Ser Asn Val Gly	
2420 2425 2430	
cac aca cag gct gcc gcg ggc gtc gcc ggg gtg atc aag atg gtg atg	7344
His Thr Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val Met	
2435 2440 2445	
gcg ctg cgg cat ggt ctg ctg ccg cgg acg ttg cat gtg gat gag ccg	7392

Ala Leu Arg His Gly Leu Leu Pro Arg Thr Leu His Val Asp Glu Pro
 2450 2455 2460

tcg ccg cat gtg gac tgg tcc gcg ggt gcg gtg cag ctg ctg acg gag 7440
 Ser Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu Leu Thr Glu
 2465 2470 2475 2480

acg gtg ccc tgg ccc ggc ggg gag ggg cgg cta cgg cgg gca gga gtg 7488
 Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Leu Arg Arg Ala Gly Val
 2485 2490 2495

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 Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu
 2500 2505 2510

gca ccc gcc gac gac gtt ccg ggg gga cca ccc gcc ggc gag ggt gac 7584
 Ala Pro Ala Asp Asp Val Pro Gly Gly Pro Pro Ala Gly Glu Gly Asp
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 Ala Gly Ser Asp Asp Glu Ala Ala Ala Gly Ser Pro Gly Val Trp Pro
 2530 2535 2540

tgg ctg gtg tcg gcc aag tcg cag ccg gcc ctg cgc gcc cag gcc cag 7680
 Trp Leu Val Ser Ala Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln
 2545 2550 2555 2560

gcc ctg cac gcc cac ctc acc gac cac ccc ggc ctc gac ctc gcg gat 7728
 Ala Leu His Ala His Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp
 2565 2570 2575

gtc gga tac acc ctc gcc cac gcc cgc gcc gtg ttc gac cac cgc gcc 7776
 Val Gly Tyr Thr Leu Ala His Ala Arg Ala Val Phe Asp His Arg Ala
 2580 2585 2590

acc ctc atc gcc gcg gac cgc gac acg ttc ctg caa gca ctc cag gca 7824
 Thr Leu Ile Ala Ala Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala
 2595 2600 2605

ctc gcc gca ggc gag ccc cac ccc gcc gtc atc cac agc agc gcc ccg 7872
 Leu Ala Ala Gly Glu Pro His Pro Ala Val Ile His Ser Ser Ala Pro
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ggc ggg acc ggg acc ggg gag gcc gca gga aag acc gca ttc atc tgc 7920
 Gly Gly Thr Gly Thr Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys
 2625 2630 2635 2640

tcc gga cag ggc acc caa cgc ccc ggc atg gcc cac ggc ctc tac cac 7968
 Ser Gly Gln Gly Thr Gln Arg Pro Gly Met Ala His Gly Leu Tyr His
 2645 2650 2655

acc cac ccc gtc ttc gcc gcc gca ctc aac gac atc tgc acc cac ctc 8016
 Thr His Pro Val Phe Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu
 2660 2665 2670

gac ccc cac ctc gac cac ccc ctc ctc ccc ctc ctc acc caa aac gac 8064
 Asp Pro His Leu Asp His Pro Leu Leu Pro Leu Leu Thr Gln Asn Asp
 2675 2680 2685

aac gac aac gag gac gcg gcc gca ctg ctc cag cag acc cgc tac gcc 8112
 Asn Asp Asn Glu Asp Ala Ala Ala Leu Leu Gln Gln Thr Arg Tyr Ala
 2690 2695 2700

cag ccc gcc ctc ttc gcc ttc cag gtc gcc ctc cac cgc ctc ctc acc 8160
 Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr
 2705 2710 2715 2720

gac ggc tac cac atc acc ccc cac tac tac gcc gga cac tcc ctc ggc 8208
 Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly
 2725 2730 2735

gaa atc acc gcc gcc cac ctc gcc ggc atc ctc acc ctc acc gac gcc 8256
 Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala
 2740 2745 2750

acc acc ctc atc acc caa cgc gcc acc ctc atg caa acc atg ccc ccc 8304

Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro
 2755 2760 2765

ggc acc atg acc acc ctc cac acc acc ccc cac cac atc acc cac cac 8352
 Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His His
 2770 2775 2780

ctc acc gcc cac gaa aac gac ctc gcc atc gcc gcc atc aac acc ccc 8400
 Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro
 2785 2790 2795 2800

acc tcc ctc gtc atc agc ggc acc ccc cac acc gtc caa cac atc acc 8448
 Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr
 2805 2810 2815

acc ctc tgc caa caa caa ggc atc aaa acc aaa acc ctc ccc acc aac 8496
 Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Asn
 2820 2825 2830

cac gcc ttc cac tcc ccc cac acc aac ccc atc ctc aac caa ctc cac 8544
 His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His
 2835 2840 2845

cag cac acc caa acc ctc acc tac cac cca ccc cac acc ccc ctc atc 8592
 Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile
 2850 2855 2860

acc gcc aac acc cca ccc gac caa ctc ctc acc ccc cac tac tgg acc 8640
 Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr
 2865 2870 2875 2880

caa caa gcc cgc aac acc gtc gac tac gcc acc acc acc caa acc ctc 8688
 Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr Leu
 2885 2890 2895

cac caa cac ggc gtc acc acc tac atc gaa ctc gga ccc gac aac acc 8736
 His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr
 2900 2905 2910

ctc acc acc ctc acc cac cac aac ctc ccc aac ccc ccc acc acc acc 8784
 Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Pro Pro Thr Thr Thr
 2915 2920 2925

ctc acc ctc acc cac ccc cac cac cac ccc caa acc cac ctc ctc acc 8832
 Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu Thr
 2930 2935 2940

aac ctc gcc aaa acc acc acc acc tgg cac ccc cac cac tac acc cac 8880
 Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr His
 2945 2950 2955 2960

cac gac aac caa ccc cac acc cac acc cac ctc gac ctc ccc acc tac 8928
 His Asp Asn Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr
 2965 2970 2975

ccc ttc caa cac cac cac tac tgg ctc gaa agc aca cag ccc ggt gcc 8976
 Pro Phe Gln His His His Tyr Trp Leu Glu Ser Thr Gln Pro Gly Ala
 2980 2985 2990

ggc aac gtg tca gca gcc gga ctc gac ccc acc gaa cac ccc cta ctc 9024
 Gly Asn Val Ser Ala Ala Gly Leu Asp Pro Thr Glu His Pro Leu Leu
 2995 3000 3005

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 Gly Ala Thr Leu Glu Leu Ala Thr Asp Gly Gly Ala Leu Leu Ala Gly
 3010 3015 3020

cgc ttg tct ttg agg tgc cat ccg tgg ctg gct gac cat gcc gtc ggc 9120
 Arg Leu Ser Leu Arg Ser His Pro Trp Leu Ala Asp His Ala Val Gly
 3025 3030 3035 3040

ggc acg gtg ctg ctg tgc ggc gcc acc ttc ctc gaa ctc gcc ctt cat 9168
 Gly Thr Val Leu Leu Ser Gly Ala Thr Phe Leu Glu Leu Ala Leu His
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0914286-083404

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ttc ggg gag ggt gtt cgg gtg ccg gct gtg tgg ggt ggt gtg tcg ctt 9744
Phe Gly Glu Gly Val Arg Val Pro Ala Val Trp Gly Gly Val Ser Leu
3235 3240 3245

cac cgg gcg ggt gtg acc ggt gtg cgg gtg cgt gtg tcg gct gtc ggg 9792
His Arg Ala Gly Val Thr Gly Val Arg Val Arg Val Ser Ala Val Gly
3250 3255 3260

cgg ggc ggc ggg cgt gag gcg gtg tcg gtc gtg gtc ggg gat gag gcg 9840
Arg Gly Gly Gly Arg Glu Ala Val Ser Val Val Val Gly Asp Glu Ala
3265 3270 3275 3280

ggt gtg ccg gtg gcg tcg gtc gat cgt ctt gag ttg cgg cct gtg gat 9888
Gly Val Pro Val Ala Ser Val Asp Arg Leu Glu Leu Arg Pro Val Asp
3285 3290 3295

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Met Gly Gln Leu Arg Ala Val Ser Val Ser Ala Gly Arg Arg Gly Ser
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Leu Tyr Ala Val Gln Trp Ala Glu Val Gly Pro Val Pro Val Cys Gly
3315 3320 3325

cag gcg tgg gcg tgg cac gag gac gtg ggt gag agc ggt ggt ggg cct 10032
Gln Ala Trp Ala Trp His Glu Asp Val Gly Glu Ser Gly Gly Gly Pro
3330 3335 3340

gtg ccg ggg gtg gtg gtg ttg cgg tgc ccg gat gcc ggt gcc ggt ggc 10080
Val Pro Gly Val Val Val Leu Arg Cys Pro Asp Ala Gly Ala Gly Gly
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ggt ggc ggt ggc ggt ggt ggc ggt ggt gtg ggt gag gtt gtt ggt ggg 10128

Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Val Gly Glu Val Val Gly Gly
 3365 3370 3375

gtg ttg ggt gtg gtg cag ggg tgg ctg ggg ctg gag cgg ttt gcg ggt 10176
 Val Leu Gly Val Val Gln Gly Trp Leu Gly Leu Glu Arg Phe Ala Gly
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 Ser Arg Leu Val Val Val Thr Arg Gly Ala Val Val Ala Gly Pro Glu
 3395 3400 3405

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 Asp Gly Pro Val Asp Val Val Gly Ala Ser Val Trp Gly Leu Val Arg
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 Val Asp Gly Gly Arg Val Ala Ala Val Val Ala Cys Gly Glu Pro Gln
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 Leu Ala Val Arg Gly Glu Arg Leu Leu Ala Ala Arg Leu Lys Arg Leu
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 3490 3495 3500

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 Arg Arg Ser Asp Val Pro Ala Gln Arg Ser Gly Gly Val Pro Ala Arg
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Arg Ser Val Asp Val Ser Gly Arg Glu Val Leu Pro Trp Leu Ser Gly	
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Gly Ser Val Leu Val Thr Gly Gly Thr Gly Val Leu Gly Ala Ala Val	
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Ala Arg His Leu Ala Gly Val Cys Gly Val Arg Asp Leu Leu Leu Val	
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Ser Arg Arg Gly Pro Asp Ala Pro Gly Ala Glu Gly Leu Arg Ala Glu	
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Leu Ala Ala Leu Gly Ala Glu Val Arg Ile Val Ala Cys Asp Val Gly	
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Glu Arg Arg Glu Val Val Arg Leu Leu Glu Gly Val Pro Ala Gly Cys	
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Pro Leu Thr Gly Val Val His Ala Ala Gly Val Leu Asp Asp Ala Thr	
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Ile Ala Ser Leu Thr Pro Glu Arg Leu Gly Thr Val Phe Ala Ala Lys	
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Val Asp Ala Ala Leu Leu Leu Asp Glu Leu Thr Arg Gly Met Glu Leu	
3650 3655 3660	
tcg gcg ttc gtg ctg ttc tcc tcg gcc gcg ggg atc ctg ggg tcg gcc	11040

Ser Ala Phe Val Leu Phe Ser Ser Ala Ala Gly Ile Leu Gly Ser Ala
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 3685 3690 3695

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 Tyr Arg Arg Arg Ala Ala Gly Leu Pro Gly Val Ser Leu Ala Trp Gly
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ctg tgg gaa gag gcc agc ggg atg acc ggg cac ctg gcc ggc acc gac 11184
 Leu Trp Glu Glu Ala Ser Gly Met Thr Gly His Leu Ala Gly Thr Asp
 3715 3720 3725

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 Leu Pro Ala Asp Leu Arg Pro Ala Pro Pro Leu Pro Pro Leu Leu Gln
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 Asp Leu Leu Pro Ala Thr Arg Arg Arg Thr Thr Arg Thr Thr Thr
 3780 3785 3790

ggt ggt gcg gac aac ggc gcc cag ctg cac gcc cgg ctg gcc ggc cag 11424
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 3795 3800 3805

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 Thr His Glu Gln Gln His Thr Thr Leu Leu Ala Leu Val Arg Ser His
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 Ile Ala Thr Val Leu Gly His Thr Thr Pro Asp Thr Ile Pro Pro Asp
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 3845 3850 3855

cgc aac cgg ctc tcc cgc acc acc gga ctc cgc ctc ccc acc acc ctc 11616
 Arg Asn Arg Leu Ser Arg Thr Thr Gly Leu Arg Leu Pro Thr Thr Leu
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gcc ttc gac cac ccc aac ccc acc acc ctc acc cac cac ctc cac aca 11664
 Ala Phe Asp His Pro Asn Pro Thr Thr Leu Thr His His Leu His Thr
 3875 3880 3885

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 Gln Leu Gln Pro Gln Pro Asp Asn Ala Val Ala Pro Val Leu Ala Glu
 3890 3895 3900

ctc gac aaa ctc gaa tcc gcc ctc tcc gcc ctc gac aaa acc gac agc 11760
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 Ala Ser Glu Arg Val Thr Leu Arg Leu Lys Ser Leu Met Leu Arg Trp
 3925 3930 3935

aac gca ccc cag cat ccg aca gcc gaa agc gct gat gac gac gag aag 11856
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 Phe Thr Ser Ala Thr Glu Ala Glu Ile Phe Lys Phe Ile Asp Asn Asp
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3970

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Met Gln Leu Ala Asn Glu Ala Lys Leu Leu Glu Tyr
3975 3980

ctc aag cgc gtc act gcg gac ctg gac cgc act cgc cgt cgc ctg tac 12054
Leu Lys Arg Val Thr Ala Asp Leu Asp Arg Thr Arg Arg Arg Leu Tyr
3985 3990 3995 4000

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Glu Val Val Glu Arg Glu Gln Glu Pro Ile Ala Ile Val Gly Met Ala
4005 4010 4015

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Cys Arg Tyr Pro Gly Gly Ala Thr Ser Pro Thr Arg Leu Trp His Leu
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Val Lys Ser Gln Thr Asp Ala Ile Gly Glu Phe Pro Thr Asp Arg Gly
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Trp Asn Leu Glu Gln Leu Tyr Asp Pro Asp Pro Asp Arg Ser Gly Thr
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Ser Tyr Thr Arg Ser Gly Gly Phe Leu Tyr Asp Ala Gly Asp Phe Asp
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Gln Gln Arg Leu Leu Leu Glu Thr Thr Trp Glu Thr Phe Glu Gln Gly
4100 4105 4110

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Gly Ile Asp Pro Arg Ser Met Arg Gly Ser Arg Thr Gly Val Phe Val	
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Gly Ile Asn Pro Glu Asp Tyr Thr Thr Gly Tyr Thr His Gln Pro Ser	
4130 4135 4140	
aac gca gtc gag ggc tac ctg ctc act ggc agc gcg gca agc att gcg	12534
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4145 4150 4155 4160	
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Ser Gly Arg Ile Ser Tyr Asn Phe Gly Leu Glu Gly Pro Ala Ile Thr	
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Ile Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys	
4180 4185 4190	
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Gln Ala Leu Arg Ser Gly Glu Cys Thr Met Ala Leu Ala Gly Gly Ala	
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Ser Val Met Ala Thr Pro Phe Val Phe Thr Glu Phe Ser Arg Gln Arg	
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4225 4230 4235 4240	
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Gly Thr Gly Trp Ser Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu	
4245 4250 4255	
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Ser Asp Ala Arg Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly
 4260 4265 4270

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 4275 4280 4285

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 4290 4295 4300

ctc tcc cct gcc gat gtc gat gcg gtg gag gcc cac ggc acg ggg acc 13014
 Leu Ser Pro Ala Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr
 4305 4310 4315 4320

acc ctg ggc gac ccg atc gag gct caa gcc ctc gtc gaa gcc tac ggt 13062
 Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Val Glu Ala Tyr Gly
 4325 4330 4335

cag gac cgc ccc aac ggc cgc ccc ctc tgg ctc gga acc ctc aag tcc 13110
 Gln Asp Arg Pro Asn Gly Arg Pro Leu Trp Leu Gly Thr Leu Lys Ser
 4340 4345 4350

aac atc ggg cac tcc atg gcc gct gcg ggt gtg ggc ggg gtc atc aag 13158
 Asn Ile Gly His Ser Met Ala Ala Ala Gly Val Gly Gly Val Ile Lys
 4355 4360 4365

atg gtg atg gcg ctg cgg aat ggt ctg ctg ccg cgg acg ttg cat gtg 13206
 Met Val Met Ala Leu Arg Asn Gly Leu Leu Pro Arg Thr Leu His Val
 4370 4375 4380

gat gag ccg tcg ccg cat gtg gac tgg tcc gcg ggt gcg gtg cag ctg 13254
 Asp Glu Pro Ser Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu
 4385 4390 4395 4400

ctg acg gag acg gtg ccc tgg ccc ggc ggg gag ggg cgg cta cgg cgg 13302
 Leu Thr Glu Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Leu Arg Arg
 4405 4410 4415

00914286 002401

gca gga gtg tca tca ttc ggc gtc agc ggc acc aac gcc cac gtc atc 13350
Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile
4420 4425 4430

ctc gag gaa gca ccc gcc cac aac atc ccg tca gac aca ccc gcc gac 13398
Leu Glu Glu Ala Pro Ala His Asn Ile Pro Ser Asp Thr Pro Ala Asp
4435 4440 4445

gac gtc ccg gga gaa tca gcc gcc gac gag gat gcc ggt agt ggc gat 13446
Asp Val Pro Gly Glu Ser Ala Ala Asp Glu Asp Ala Gly Ser Gly Asp
4450 4455 4460

gag gct gct gcc ggc agt cca ggg gtg tgg ccg tgg ctg gtg tcg gcc 13494
Glu Ala Ala Ala Gly Ser Pro Gly Val Trp Pro Trp Leu Val Ser Ala
4465 4470 4475 4480

aag tcg cag ccg gcc ctg cgc gcc cag gcc cag gcc ctg cac gcc cac 13542
Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln Ala Leu His Ala His
4485 4490 4495

ctc acc gac cac ccc ggc ctc gac ctc gcc gac gtc ggg tac acc ctc 13590
Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp Val Gly Tyr Thr Leu
4500 4505 4510

gcc cac gcc cgc gcc gtg ttc gac cac cgc gcc acc ctc atc gcc gcc 13638
Ala His Ala Arg Ala Val Phe Asp His Arg Ala Thr Leu Ile Ala Ala
4515 4520 4525

gac cgc gac acc ttc ctg caa gca ctc cag gca ctc gcc gca ggc gaa 13686
Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala Leu Ala Ala Gly Glu
4530 4535 4540

ccc cac ccc gcc gtc atc cac agc agc gcc cca ggc ggg acc ggg acc 13734
Pro His Pro Ala Val Ile His Ser Ser Ala Pro Gly Gly Thr Gly Thr
4545 4550 4555 4560

ggg gag gcc gca gga aag acc gca ttc atc tgc tcc gga cag ggc acc 13782

Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys Ser Gly Gln Gly Thr
 4565 4570 4575

caa cgc ccc ggc atg gcc cac ggc ctc tac cac acc cac ccc gtc ttc 13830
 Gln Arg Pro Gly Met Ala His Gly Leu Tyr His Thr His Pro Val Phe
 4580 4585 4590

gcc gcc gca ctc aac gac atc tgc acc cac ctc gac ccc cac ctc gac 13878
 Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu Asp Pro His Leu Asp
 4595 4600 4605

cac ccc ctc ctc ccc ctc ctc acc cag gac ccc aac acc cag gac acc 13926
 His Pro Leu Leu Pro Leu Leu Thr Gln Asp Pro Asn Thr Gln Asp Thr
 4610 4615 4620

acc acc ctc gaa gaa gcg gcc gca ctg ctc cag cag acc cgc tac gcc 13974
 Thr Thr Leu Glu Glu Ala Ala Ala Leu Leu Gln Gln Thr Arg Tyr Ala
 4625 4630 4635 4640

cag ccc gcc ctc ttc gcc ttc cag gtc gcc ctc cac cgc ctc ctc acc 14022
 Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr
 4645 4650 4655

gac ggc tac cac atc acc ccc cac tac tac gcc gga cac tcc ctc ggc 14070
 Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly
 4660 4665 4670

gaa atc acc gcc gcc cac ctc gcc ggc atc ctc acc ctc acc gac gcc 14118
 Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala
 4675 4680 4685

acc acc ctc atc acc caa cgc gcc acc ctc atg caa acc atg ccc ccc 14166
 Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro
 4690 4695 4700

ggc acc atg acc acc ctc cac acc acc ccc cac cac atc acc cac cac 14214
 Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His His
 4705 4710 4715 4720

ctc acc gcc cac gaa aac gac ctc gcc atc gcc gcc atc aac acc ccc	14262
Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro	
4725 4730 4735	
acc tcc ctc gtc atc agc ggc acc ccc cac acc gtc caa cac atc acc	14310
Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr	
4740 4745 4750	
acc ctc tgc caa caa caa ggc atc aaa acc aaa acc ctc ccc acc aac	14358
Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Asn	
4755 4760 4765	
cac gcc ttc cac tcc ccc cac acc aac ccc atc ctc aac caa ctc cac	14406
His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His	
4770 4775 4780	
cag cac acc caa acc ctc acc tac cac cca ccc cac acc ccc ctc atc	14454
Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile	
4785 4790 4795 4800	
acc gcc aac acc cca ccc gac caa ctc ctc acc ccc cac tac tgg acc	14502
Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr	
4805 4810 4815	
caa caa gcc cgc aac acc gtc gac tac gcc acc acc acc caa acc ctc	14550
Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr Leu	
4820 4825 4830	
cac caa cac ggc gtc acc acc tac atc gaa ctc gga ccc gac aac acc	14598
His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr	
4835 4840 4845	
ctc acc acc ctc acc cac gac aac ctc ccc aac acc ccc acc acc acc	14646
Leu Thr Thr Leu Thr His Asp Asn Leu Pro Asn Thr Pro Thr Thr Thr	
4850 4855 4860	
ctc acc ctc acc cac ccc cac cac cac ccc caa acc cac ctc ctc acc	14694

Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu Thr
 4865 4870 4875 4880

aac ctc gcc aaa acc acc acc acc tgg cac ccc cac cac tac acc cac 14742
 Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr His
 4885 4890 4895

cac cac aac caa ccc cac acc cac acc cac ctc gac ctc ccc acc tac 14790
 His His Asn Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr
 4900 4905 4910

ccc ttc caa cac cac cac tac tgg ctc caa cca ccc ggc aag ccg agc 14838
 Pro Phe Gln His His His Tyr Trp Leu Gln Pro Pro Gly Lys Pro Ser
 4915 4920 4925

gac ccg tca ccg agc gaa ggc cgt gag caa gcc acg acc cca tca acc 14886
 Asp Pro Ser Pro Ser Glu Gly Arg Glu Gln Ala Thr Thr Pro Ser Thr
 4930 4935 4940

ccg ctg cgt gat gtc ctc gtg ggc aag tct ccg cag gag cga gac gaa 14934
 Pro Leu Arg Asp Val Leu Val Gly Lys Ser Pro Gln Glu Arg Asp Glu
 4945 4950 4955 4960

gag ctg ttg cgc ctg gtg cgc acc cat gcg gcc gct gtg ctg ggc cat 14982
 Glu Leu Leu Arg Leu Val Arg Thr His Ala Ala Ala Val Leu Gly His
 4965 4970 4975

gcc act ccc gaa gtg atc gtt ccg aac aag gcc ttc aaa gag ctg ggt 15030
 Ala Thr Pro Glu Val Ile Val Pro Asn Lys Ala Phe Lys Glu Leu Gly
 4980 4985 4990

ttt gat tct ctc gcc gca att cag ctt cgt aat cga ctg ctt gct gac 15078
 Phe Asp Ser Leu Ala Ala Ile Gln Leu Arg Asn Arg Leu Leu Ala Asp
 4995 5000 5005

gtt gac ctg ccg ctt ccg gcc acg ctg atc ttc gat tac ccc act ccg 15126
 Val Asp Leu Pro Leu Pro Ala Thr Leu Ile Phe Asp Tyr Pro Thr Pro
 5010 5015 5020

09914286 003401

atg gcg ctt tgc cag ttc ctc cgg gcg gcg atc gtc gga gcg gac aca 15174
Met Ala Leu Cys Gln Phe Leu Arg Ala Ala Ile Val Gly Ala Asp Thr
5025 5030 5035 5040

ggc acg acc act cgt ctg ccg cta act gcg gtc ccc gcc gac gag ccg 15222
Gly Thr Thr Thr Arg Leu Pro Leu Thr Ala Val Pro Ala Asp Glu Pro
5045 5050 5055

atc gcc atc gtc ggc atg gcc tgt cgg tac ccc ggt gat gta cgg acg 15270
Ile Ala Ile Val Gly Met Ala Cys Arg Tyr Pro Gly Asp Val Arg Thr
5060 5065 5070

gtc gat gat ctc tgg cag gtg gtc agt ggt ggc cat gac gcg atc ggc 15318
Val Asp Asp Leu Trp Gln Val Val Ser Gly Gly His Asp Ala Ile Gly
5075 5080 5085

gga ttc ccg acg aac cgt ggg tgg gac ctc gac acg ctg tac aac ccg 15366
Gly Phe Pro Thr Asn Arg Gly Trp Asp Leu Asp Thr Leu Tyr Asn Pro
5090 5095 5100

gac ccg gac cac cac gga acc agc tac acc cgg agc ggc gga ttc ctt 15414
Asp Pro Asp His His Gly Thr Ser Tyr Thr Arg Ser Gly Gly Phe Leu
5105 5110 5115 5120

tac gac gca ggc aat ttc gat ccc gac ttc ttc ggt atc agt ccg cgt 15462
Tyr Asp Ala Gly Asn Phe Asp Pro Asp Phe Phe Gly Ile Ser Pro Arg
5125 5130 5135

gag gca ctg gcg atg gac ccg cag cag cgg ctg ctg ctg gaa aca gcg 15510
Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Thr Ala
5140 5145 5150

tgg gag agc atc gaa cac gcc tgc atc aac ccc gac agc ctc cgt ggc 15558
Trp Glu Ser Ile Glu His Ala Cys Ile Asn Pro Asp Ser Leu Arg Gly
5155 5160 5165

aca cca acc ggc gtc ttc gcc ggg ctg acc tac cac gac tac gcc gcg 15606

Thr Pro Thr Gly Val Phe Ala Gly Leu Thr Tyr His Asp Tyr Ala Ala
 5170 5175 5180

cgc ttt ccc aca gct ccg gca ggg ttc gag ggg tat ctc ggg cac gga 15654
 Arg Phe Pro Thr Ala Pro Ala Gly Phe Glu Gly Tyr Leu Gly His Gly
 5185 5190 5195 5200

agc gca ggc agt atc gcc tcg ggt cgt gtc gcc tac gct ctc ggc ctg 15702
 Ser Ala Gly Ser Ile Ala Ser Gly Arg Val Ala Tyr Ala Leu Gly Leu
 5205 5210 5215

gaa ggt ccg gcc ctc aca gtc gac act gcc tgc tct tcg tcc ctg gtc 15750
 Glu Gly Pro Ala Leu Thr Val Asp Thr Ala Cys Ser Ser Ser Leu Val
 5220 5225 5230

gct ctg cac ctg gcc tgt cag gcg ctg cgg tcc ggc gag tgt tcc atg 15798
 Ala Leu His Leu Ala Cys Gln Ala Leu Arg Ser Gly Glu Cys Ser Met
 5235 5240 5245

gcc ctc gcg ggt ggc gtc acg gtg atg tca acc ccg gcc ggg ttc gtg 15846
 Ala Leu Ala Gly Gly Val Thr Val Met Ser Thr Pro Ala Gly Phe Val
 5250 5255 5260

gag ttt tcg cgg cag cgg ggc ctg gcc gtg gac ggg cgg tgc aag gcg 15894
 Glu Phe Ser Arg Gln Arg Gly Leu Ala Val Asp Gly Arg Cys Lys Ala
 5265 5270 5275 5280

ttc tcg gca gcg gct gac ggc acc ggc tgg ggt gag ggt gtc gga atg 15942
 Phe Ser Ala Ala Ala Asp Gly Thr Gly Trp Gly Glu Gly Val Gly Met
 5285 5290 5295

ctg ctg gtg gag cgg ctg tcg gac gcg cgg cgg ctc ggt cac cga atc 15990
 Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Leu Gly His Arg Ile
 5300 5305 5310

ctc gcg gtg gtg cgt ggc agt gcg gtc aat cag gac ggt gcg agc aac 16038
 Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn
 5315 5320 5325

ggg ctg acg gcg ccc aac ggg ccg tcc cag gag cgt gtc atc cgc ctg 16086
 Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln Glu Arg Val Ile Arg Leu
 5330 5335 5340

gcc ctg gcc aac gcg gac ctg acc ccc gcc gac gtc gat gcg gtg gag 16134
 Ala Leu Ala Asn Ala Asp Leu Thr Pro Ala Asp Val Asp Ala Val Glu
 5345 5350 5355 5360

gcc cac ggc acc ggc acc act ttg ggc gac ccg atc gag gcc cag gcc 16182
 Ala His Gly Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala
 5365 5370 5375

ctc ctc gcc acc tac gga cag gac cgc ccc ggc aac gaa ccg ctg tgg 16230
 Leu Leu Ala Thr Tyr Gly Gln Asp Arg Pro Gly Asn Glu Pro Leu Trp
 5380 5385 5390

ctg ggc tcg atg aag tcg aac atc ggc cac gcg cag gct gcc gca ggt 16278
 Leu Gly Ser Met Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala Gly
 5395 5400 5405

gtg ggc ggg gtc atc aag atg gtg atg gcg ctg cgg aat ggt ctg ctg 16326
 Val Gly Gly Val Ile Lys Met Val Met Ala Leu Arg Asn Gly Leu Leu
 5410 5415 5420

ccg cgg acg ttg cat gtg gat gag ccg tcg ccg cat gtg gac tgg tcc 16374
 Pro Arg Thr Leu His Val Asp Glu Pro Ser Pro His Val Asp Trp Ser
 5425 5430 5435 5440

gcg ggg gcg gtg cag ctg ctg acg gag acg gtg ccc tgg ccc ggc ggg 16422
 Ala Gly Ala Val Gln Leu Leu Thr Glu Thr Val Pro Trp Pro Gly Gly
 5445 5450 5455

gag ggg cgg ctg cgg cgg gca gga gtg tca tcg ttc ggc gtc agc ggc 16470
 Glu Gly Arg Leu Arg Arg Ala Gly Val Ser Ser Phe Gly Val Ser Gly
 5460 5465 5470

acc aac gcc cac gtc atc ctc gaa gaa gca ccc gcc cac aac atc ccg 16518

Thr Asn Ala His Val Ile Leu Glu Glu Ala Pro Ala His Asn Ile Pro
 5475 5480 5485

tca gac aca ccc gcc gac gac gcc ccg gga gaa gca gcc gcc gac gat 16566
 Ser Asp Thr Pro Ala Asp Asp Ala Pro Gly Glu Ala Ala Ala Asp Asp
 5490 5495 5500

gtt ccg ggg gaa gcg gcc ggc gac gac gcc ggt acc ggc ggg gaa gcg 16614
 Val Pro Gly Glu Ala Ala Gly Asp Asp Ala Gly Thr Gly Gly Glu Ala
 5505 5510 5515 5520

act ggt cct gct gcc ggc agt cca ggg gtg tgg ccg tgg ctg gtg tcg 16662
 Thr Gly Pro Ala Ala Gly Ser Pro Gly Val Trp Pro Trp Leu Val Ser
 5525 5530 5535

gcc aag tcg cag ccg gcc ctg cgc gcc cag gcc cag gcc ctg cac gcc 16710
 Ala Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln Ala Leu His Ala
 5540 5545 5550

cac ctc acc gac cac ccc ggc ctc gac ctc gcc gac gtc ggg tac acc 16758
 His Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp Val Gly Tyr Thr
 5555 5560 5565

ctc gcc cac gcc cgc gcc gtg ttc gac cac cgc gcc acc ctc atc gcc 16806
 Leu Ala His Ala Arg Ala Val Phe Asp His Arg Ala Thr Leu Ile Ala
 5570 5575 5580

gcc gac cgc gac acc ttc ctg caa gca ctc cag gca ctc gcc gca ggc 16854
 Ala Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala Leu Ala Ala Gly
 5585 5590 5595 5600

gaa ccc cac ccc gcc gtc atc cac agc agc gcc cca ggc ggg acc ggg 16902
 Glu Pro His Pro Ala Val Ile His Ser Ser Ala Pro Gly Gly Thr Gly
 5605 5610 5615

acc ggg gag gcc gca gga aag acc gca ttc atc tgc tcc gga cag ggc 16950
 Thr Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys Ser Gly Gln Gly
 5620 5625 5630

acc caa cgc ccc ggc atg gcc cac ggc ctc tac cac acc cac ccc gtc 16998
 Thr Gln Arg Pro Gly Met Ala His Gly Leu Tyr His Thr His Pro Val
 5635 5640 5645

ttc gcc gcc gca ctc aac gac atc tgc acc cac ctc gac ccc cac ctc 17046
 Phe Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu Asp Pro His Leu
 5650 5655 5660

gac cac ccc ctc ctc ccc ctc ctc acc cag gac ccc aac acc cag gac 17094
 Asp His Pro Leu Leu Pro Leu Leu Thr Gln Asp Pro Asn Thr Gln Asp
 5665 5670 5675 5680

acc acc acc ctc gaa gaa gcg gcc gca ctg ctc cag cag acc ccg tac 17142
 Thr Thr Thr Leu Glu Glu Ala Ala Ala Leu Leu Gln Gln Thr Pro Tyr
 5685 5690 5695

gcc cag ccc gcc ctc ttc gcc ttc cag gtc gcc ctc cac cgc ctc ctc 17190
 Ala Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu
 5700 5705 5710

acc gac ggc tac cac atc acc ccc cac tac tac gcc gga cac tcc ctc 17238
 Thr Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu
 5715 5720 5725

ggc gaa atc acc gcc gcc cac ctc gcc ggc atc ctc acc ctc acc gac 17286
 Gly Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp
 5730 5735 5740

gcc acc acc ctc atc acc caa cgc gcc acc ctc atg caa acc atg ccc 17334
 Ala Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro
 5745 5750 5755 5760

ccc ggc acc atg acc acc ctc cac acc acc ccc cac cac atc acc cac 17382
 Pro Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His
 5765 5770 5775

cac ctc acc gcc cac gaa aac gac ctc gcc atc gcc gcc atc aac acc 17430

His Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr
5780 5785 5790

ccc acc tcc ctc gtc atc agc ggc acc ccc cac acc gtc caa cac atc 17478
Pro Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile
5795 5800 5805

acc acc ctc tgc caa caa caa ggc atc aaa acc aaa acc ctc ccc acc 17526
Thr Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr
5810 5815 5820

aaa aac gcc ttc cac tcc ccc cac acc aac ccc atc ctc aac caa ctc 17574
Lys Asn Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu
5825 5830 5835 5840

cac cag cac acc caa acc ctc acc tac cac cca ccc cac acc ccc ctc 17622
His Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu
5845 5850 5855

atc acc gcc aac acc cca ccc gac caa ctc ctc acc ccc cac tac tgg 17670
Ile Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp
5860 5865 5870

acc caa caa gcc cgc aac acc gtc gac tac gcc acc acc acc caa acc 17718
Thr Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr
5875 5880 5885

ctc cac caa cac ggc gtc acc acc tac atc gaa ctc gga ccc gac aac 17766
Leu His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn
5890 5895 5900

acc ctc acc acc ctc acc cac cac aac ctc ccc aac acc ccc acc acc 17814
Thr Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Thr Pro Thr Thr
5905 5910 5915 5920

acc ctc acc ctc acc cac ccc cac cac cac ccc caa acc cac ctc ctc 17862
Thr Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu
5925 5930 5935

acc aac ctc gcc aaa acc acc acc acc tgg cac ccc cac cac tac acc	17910
Thr Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr	
5940 5945 5950	
cac cac cac aac caa ccc cac acc cac acc cac ctc gac ctc ccc acc	17958
His His His Asn Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr	
5955 5960 5965	
tac ccc ttc caa cac cag cac tac tgg ctc gaa agc aca cag ccg ggt	18006
Tyr Pro Phe Gln His Gln His Tyr Trp Leu Glu Ser Thr Gln Pro Gly	
5970 5975 5980	
gcc gga tcc ggt tcc ggt tcc ggt tcc ggg cgg gca ggg act gcg ggc	18054
Ala Gly Ser Gly Ser Gly Ser Gly Ser Gly Arg Ala Gly Thr Ala Gly	
5985 5990 5995 6000	
ggg acg gca gag gtg gag tcc cgg ttc tgg gac gcg gtg gcc cgc cag	18102
Gly Thr Ala Glu Val Glu Ser Arg Phe Trp Asp Ala Val Ala Arg Gln	
6005 6010 6015	
gac ctg gaa acg gtc gcg acc acg ctc gcc gtg ccc ccc tcc gcc ggc	18150
Asp Leu Glu Thr Val Ala Thr Thr Leu Ala Val Pro Pro Ser Ala Gly	
6020 6025 6030	
ctg gac acg gtg gtg ccc gca ctc tcc gcc tgg cac cgc cac caa cac	18198
Leu Asp Thr Val Val Pro Ala Leu Ser Ala Trp His Arg His Gln His	
6035 6040 6045	
gac caa gcc cgc atc aac acc tgg acc tac cag gaa acc tgg aaa ccc	18246
Asp Gln Ala Arg Ile Asn Thr Trp Thr Tyr Gln Glu Thr Trp Lys Pro	
6050 6055 6060	
ctc acc ctc ccc acc acc cac caa ccc cac caa acc tgg ctc atc gcc	18294
Leu Thr Leu Pro Thr Thr His Gln Pro His Gln Thr Trp Leu Ile Ala	
6065 6070 6075 6080	
atc ccc gaa acc cag acc cac cac ccc cac atc acc aac atc ctc acc	18342

Ile Pro Glu Thr Gln Thr His His Pro His Ile Thr Asn Ile Leu Thr
6085 6090 6095

aac ctc cac cac cac ggc atc acc ccc atc ccc ctc acc ctc aac cac 18390
Asn Leu His His His Gly Ile Thr Pro Ile Pro Leu Thr Leu Asn His
6100 6105 6110

acc cac acc aac ccc caa cac ctc cac cac acc cga caa caa gcc caa 18438
Thr His Thr Asn Pro Gln His Leu His His Thr Arg Gln Gln Ala Gln
6115 6120 6125

aac cac acc acc gga ccc atc acc ggc ctg ctc tcc ctc ctc gcc ctc 18486
Asn His Thr Thr Gly Pro Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu
6130 6135 6140

gac gaa aca ccc cac ccc cac cac ccc cac aca ccc acc ggc acc ctc 18534
Asp Glu Thr Pro His Pro His His Pro His Thr Pro Thr Gly Thr Leu
6145 6150 6155 6160

ctc aac ctc acc ctc acc caa acc cac acc caa acc cac cca cca acc 18582
Leu Asn Leu Thr Leu Thr Gln Thr His Thr Gln Thr His Pro Pro Thr
6165 6170 6175

ccc ctc tgg tac gcc acc acc aac gcc acc acc acc cac ccc aac gac 18630
Pro Leu Trp Tyr Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp
6180 6185 6190

ccc ctc aca cac ccc acc caa gcc caa acc tgg gga ctc gcc cgc acc 18678
Pro Leu Thr His Pro Thr Gln Ala Gln Thr Trp Gly Leu Ala Arg Thr
6195 6200 6205

acc ctc ctc gaa cac ccc acc cac acc gcc gga atc atc gac ctc ccc 18726
Thr Leu Leu Glu His Pro Thr His Thr Ala Gly Ile Ile Asp Leu Pro
6210 6215 6220

acc acc ccc acc ccc cac acc ctc cac cac ctc acc caa acc ctc acc 18774
Thr Thr Pro Thr Pro His Thr Leu His His Leu Thr Gln Thr Leu Thr
6225 6230 6235 6240

caa ccc cac cac caa acc caa ctc gcc atc cgc acc acc ggc acc cac 18822
 Gln Pro His His Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His
 6245 6250 6255

acc cgc cgc ctc acc ccc acc acc ctc acc ccc aca cac caa cca ccc 18870
 Thr Arg Arg Leu Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro
 6260 6265 6270

acc ccc acc ccc cac gga acc acc ctc atc acc ggc gga acc ggc gcc 18918
 Thr Pro Thr Pro His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala
 6275 6280 6285

ctc gcc acc cac ctc acc cac cac ctc acc acc cac caa ccc acc caa 18966
 Leu Ala Thr His Leu Thr His His Leu Thr Thr His Gln Pro Thr Gln
 6290 6295 6300

cac ctc ctc ctc acc agc cga acc ggc ccc cac acc ccc cac gca caa 19014
 His Leu Leu Leu Thr Ser Arg Thr Gly Pro His Thr Pro His Ala Gln
 6305 6310 6315 6320

cac ctc acc acc caa ctc caa caa aaa ggc atc cac ctc acc atc acc 19062
 His Leu Thr Thr Gln Leu Gln Gln Lys Gly Ile His Leu Thr Ile Thr
 6325 6330 6335

acc tgc gac acc agc aac cca gac caa ctc caa caa ctc ctc aac acc 19110
 Thr Cys Asp Thr Ser Asn Pro Asp Gln Leu Gln Gln Leu Leu Asn Thr
 6340 6345 6350

atc ccc cca caa cac ccc ctc acc acc gtc atc cac acc gca ggc atc 19158
 Ile Pro Pro Gln His Pro Leu Thr Thr Val Ile His Thr Ala Gly Ile
 6355 6360 6365

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 Leu Asp Asp Ala Thr Leu Thr Asn Leu Thr Pro Thr Gln Leu Asn Asn
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gtc ctc cgc gcc aaa gcc cac agc gcc cac ctc ctc cac caa ctc acc 19254

00014286 000101

Val Leu Arg Ala Lys Ala His Ser Ala His Leu Leu His Gln Leu Thr
 6385 6390 6395 6400

caa cac acc ccc ctc aac gcc ttc gtc ctc tac tcc tcc gcc gcc gcc 19302
 Gln His Thr Pro Leu Asn Ala Phe Val Leu Tyr Ser Ser Ala Ala Ala
 6405 6410 6415

acc ttc ggc gca ccc ggc caa gcc aac tac gcc gca gcc aac gcc tac 19350
 Thr Phe Gly Ala Pro Gly Gln Ala Asn Tyr Ala Ala Ala Asn Ala Tyr
 6420 6425 6430

ctc gac gcc ctc gcc cac cac cgc cac acc cac cac ctc ccc gcc acc 19398
 Leu Asp Ala Leu Ala His His Arg His Thr His His Leu Pro Ala Thr
 6435 6440 6445

agc atc gcc tgg ggc acc tgg caa gga aac gga ctg gcg act ggt caa 19446
 Ser Ile Ala Trp Gly Thr Trp Gln Gly Asn Gly Leu Ala Thr Gly Gln
 6450 6455 6460

gtc agc gaa cat ctc cgc cgc cgc ggg atg ttc gcc atg ccg ccc gag 19494
 Val Ser Glu His Leu Arg Arg Arg Gly Met Phe Ala Met Pro Pro Glu
 6465 6470 6475 6480

ttg gcg gtc aca gct gtt gac ggc gcg atc gcg agc ggg cgc ccg agt 19542
 Leu Ala Val Thr Ala Val Asp Gly Ala Ile Ala Ser Gly Arg Pro Ser
 6485 6490 6495

ctc ctc gtc gcc gat atc gac tgg aag aaa ttg gga ccg gtt ctc tcc 19590
 Leu Leu Val Ala Asp Ile Asp Trp Lys Lys Leu Gly Pro Val Leu Ser
 6500 6505 6510

agc aag tcg tcg gtc ttg ctc gag gac ctt ccc cag gca cag gga act 19638
 Ser Lys Ser Ser Val Leu Leu Glu Asp Leu Pro Gln Ala Gln Gly Thr
 6515 6520 6525

gag gag gcg cgc agt acc gtt gag cag acg gag agc aca aac ctc cgg 19686
 Glu Glu Ala Arg Ser Thr Val Glu Gln Thr Glu Ser Thr Asn Leu Arg
 6530 6535 6540

caa ctc ctc atg ggt cgg tca cgt tcc gag cag gaa gaa gag ctg ctc	19734
Gln Leu Leu Met Gly Arg Ser Arg Ser Glu Gln Glu Glu Glu Leu Leu	
6545 6550 6555 6560	
agc ctc gtc cgc atc cac tcc gcg gca gtg ctc ggg cgc gac gac tcc	19782
Ser Leu Val Arg Ile His Ser Ala Ala Val Leu Gly Arg Asp Asp Ser	
6565 6570 6575	
gag gcc atc ccg ccc ggt cgg ctg ttc agg gat cta ggg ttc gac tcg	19830
Glu Ala Ile Pro Pro Gly Arg Leu Phe Arg Asp Leu Gly Phe Asp Ser	
6580 6585 6590	
ctt gcg gcg gtg gag ctt cgc aac cac ctc gca gca cag acg gag ctg	19878
Leu Ala Ala Val Glu Leu Arg Asn His Leu Ala Ala Gln Thr Glu Leu	
6595 6600 6605	
gct ctg ccg acg act ctc gtc ttc gat tac ccc agc ccc acc aag ctc	19926
Ala Leu Pro Thr Thr Leu Val Phe Asp Tyr Pro Ser Pro Thr Lys Leu	
6610 6615 6620	
gcc caa ttt ctg ctc tcc gag atc gcg gag ttc cag ccc gac aac tca	19974
Ala Gln Phe Leu Leu Ser Glu Ile Ala Glu Phe Gln Pro Asp Asn Ser	
6625 6630 6635 6640	
act ccg ctt ccg cga ccc cgg gca gag ctc gat gag ccg atc gcc atc	20022
Thr Pro Leu Pro Arg Pro Arg Ala Glu Leu Asp Glu Pro Ile Ala Ile	
6645 6650 6655	
gtt ggc atg gcc tgt cgc ttc ccc ggc gga gtg acc tcg gcg gac gac	20070
Val Gly Met Ala Cys Arg Phe Pro Gly Gly Val Thr Ser Ala Asp Asp	
6660 6665 6670	
ttc tgg gat ctg atc tcc tcc gag cag gac gcg atc ggc gga ttc ccc	20118
Phe Trp Asp Leu Ile Ser Ser Glu Gln Asp Ala Ile Gly Gly Phe Pro	
6675 6680 6685	
acc gac cgc ggc tgg gac ctg gac acg ctc tac gac ccc gac ccc gac	20166

Thr Asp Arg Gly Trp Asp Leu Asp Thr Leu Tyr Asp Pro Asp Pro Asp
 6690 6695 6700

cac ccc ggc acc tgc tac acc cga aac ggc gga ttc ctc tac gac gca 20214
 His Pro Gly Thr Cys Tyr Thr Arg Asn Gly Gly Phe Leu Tyr Asp Ala
 6705 6710 6715 6720

ggc cac ttc gac gcc gaa ttc ttc ggc atc agc ccc cgc gaa gcc ctc 20262
 Gly His Phe Asp Ala Glu Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu
 6725 6730 6735

gcc atg gac ccc cag caa cga ctc ctc ctc gaa acc gcc tgg gaa acc 20310
 Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Thr Ala Trp Glu Thr
 6740 6745 6750

atc gaa cac gcc ggc atc aac ccc cac acc ctc cac ggc acc ccc acc 20358
 Ile Glu His Ala Gly Ile Asn Pro His Thr Leu His Gly Thr Pro Thr
 6755 6760 6765

gga gtc ttc acc ggc acc aac gga cag gac cac gcg gca cac atc cgt 20406
 Gly Val Phe Thr Gly Thr Asn Gly Gln Asp His Ala Ala His Ile Arg
 6770 6775 6780

cag gcc ccg agc ggt acc gag gga ttc gtc ctg acc ggg gca gcc acc 20454
 Gln Ala Pro Ser Gly Thr Glu Gly Phe Val Leu Thr Gly Ala Ala Thr
 6785 6790 6795 6800

agc atc gcc tcc ggc cga atc tcc tac atc ctc ggg ttg gaa ggg cct 20502
 Ser Ile Ala Ser Gly Arg Ile Ser Tyr Ile Leu Gly Leu Glu Gly Pro
 6805 6810 6815

gcg gtc acc ctc gac aca gcg tgt tcc tcc tgc ctc gtc gcc ctg cac 20550
 Ala Val Thr Leu Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His
 6820 6825 6830

ctc gcc tgc cag tcc ctc agg tcc ggt gaa tgc acc atg gcc ttg gcc 20598
 Leu Ala Cys Gln Ser Leu Arg Ser Gly Glu Cys Thr Met Ala Leu Ala
 6835 6840 6845

09914235-032401

0904035-002401

ggc ggg gcc acg gtc atg acc acc ccg atc acc ttc acc gaa ttc gcc 20646
Gly Gly Ala Thr Val Met Thr Thr Pro Ile Thr Phe Thr Glu Phe Ala
6850 6855 6860

cgc caa cgc gga ctc gcc ccc gac ggg cgt tgc aag gcg ttc tcg gcg 20694
Arg Gln Arg Gly Leu Ala Pro Asp Gly Arg Cys Lys Ala Phe Ser Ala
6865 6870 6875 6880

gcg gct gac ggt acc ggc tgg ggt gag ggt gtg ggg atg ctg ctg gtg 20742
Ala Ala Asp Gly Thr Gly Trp Gly Glu Gly Val Gly Met Leu Leu Val
6885 6890 6895

gag cgg ctc tcc gac gcc cgc cgc aac ggt cac cgt gtc ctg gcc gtg 20790
Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly His Arg Val Leu Ala Val
6900 6905 6910

gtg cgt ggc agt gcg gtc aac cag gac ggt gcg agc aac ggt ctg acc 20838
Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr
6915 6920 6925

gcg ccc aac ggg ccc tcc cag cag cgc gtc atc cgc cag gcc ctc gcc 20886
Ala Pro Asn Gly Pro Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala
6930 6935 6940

aac gcg gac ctg acc ccc gcc gac gtc gat gcg gtg gag gcc cac ggc 20934
Asn Ala Asp Leu Thr Pro Ala Asp Val Asp Ala Val Glu Ala His Gly
6945 6950 6955 6960

acc ggc acc act ttg ggc gac ccg atc gag gcc cag gcc atc ctc gcg 20982
Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Ile Leu Ala
6965 6970 6975

acc tac gga cag gac cgt ccc ggc aac ggg ccg ttg tgg ctg ggc tcc 21030
Thr Tyr Gly Gln Asp Arg Pro Gly Asn Gly Pro Leu Trp Leu Gly Ser
6980 6985 6990

gtc aag tcc aac gtc gga cac aca cag gcc gcg gcg ggc gtg gcc gga 21078

Val Lys Ser Asn Val Gly His Thr Gln Ala Ala Ala Gly Val Ala Gly
 6995 7000 7005

gtg atc aag atg gtg atg gcc ctc cgc cac cgg aca ctc cca ccg act 21126
 Val Ile Lys Met Val Met Ala Leu Arg His Arg Thr Leu Pro Pro Thr
 7010 7015 7020

ctc cac gcg gat gag ccg tcg ccg cat gtg gac tgg tcc gcg ggt gcg 21174
 Leu His Ala Asp Glu Pro Ser Pro His Val Asp Trp Ser Ala Gly Ala
 7025 7030 7035 7040

gtg cag ctg ctg acg gag acg gtg ccc tgg ccc ggc ggg gag ggg ccg 21222
 Val Gln Leu Leu Thr Glu Thr Val Pro Trp Pro Gly Gly Glu Gly Arg
 7045 7050 7055

ccg cgg cgg gca gga gtg tca tca ttc ggc gtc agc ggc acc aac gcc 21270
 Pro Arg Arg Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala
 7060 7065 7070

cac gtc atc ctc gaa gaa gca ccc gcc gac gac gtt ccg ggg gga cca 21318
 His Val Ile Leu Glu Glu Ala Pro Ala Asp Asp Val Pro Gly Gly Pro
 7075 7080 7085

ccc gcc gac gag gat gcc ggt agt ggc gag gag gct gct gcc ggc agt 21366
 Pro Ala Asp Glu Asp Ala Gly Ser Gly Glu Glu Ala Ala Ala Gly Ser
 7090 7095 7100

cct ggg gtg tgg ccg tgg ctg gtg tcg gcc aag tcg cag ccg gcc ctg 21414
 Pro Gly Val Trp Pro Trp Leu Val Ser Ala Lys Ser Gln Pro Ala Leu
 7105 7110 7115 7120

cgc gcc cag gcc cag gcc ctg cac gcc cac ctc acc gac cac ccc ggc 21462
 Arg Ala Gln Ala Gln Ala Leu His Ala His Leu Thr Asp His Pro Gly
 7125 7130 7135

ctc gac ctc gcc gac gtc gga tac acc ctc gcc cac gcc cgc gcc gtg 21510
 Leu Asp Leu Ala Asp Val Gly Tyr Thr Leu Ala His Ala Arg Ala Val
 7140 7145 7150

ttc gac cac cgc gcc acc ctc atc gcc gcc gac cgc gac acc ttc ctg	21558
Phe Asp His Arg Ala Thr Leu Ile Ala Ala Asp Arg Asp Thr Phe Leu	
7155	7160 7165
caa gca ctc cag gca ctc gcc gca ggc gaa ccc cac ccc gcc gtc atc	21606
Gln Ala Leu Gln Ala Leu Ala Ala Gly Glu Pro His Pro Ala Val Ile	
7170	7175 7180
cac agc agc gcc cca ggc ggg acc ggg acc ggg gag gcc gca gga aag	21654
His Ser Ser Ala Pro Gly Gly Thr Gly Thr Gly Glu Ala Ala Gly Lys	
7185	7190 7195 7200
acc gca ttc atc tgc tcc gga cag ggc acc caa cgc ccc ggc atg gcc	21702
Thr Ala Phe Ile Cys Ser Gly Gln Gly Thr Gln Arg Pro Gly Met Ala	
7205	7210 7215
cac ggc ctc tac cac acc cac ccc gtc ttc gcc gcc gca ctc aac gac	21750
His Gly Leu Tyr His Thr His Pro Val Phe Ala Ala Ala Leu Asn Asp	
7220	7225 7230
atc tgc acc cac ctc gac ccc cac ctc gac cac ccc ctc ctc ccc ctc	21798
Ile Cys Thr His Leu Asp Pro His Leu Asp His Pro Leu Leu Pro Leu	
7235	7240 7245
ctc acc caa aac gac aac gac aac gac aac gag gac gcg gcc gca ctg	21846
Leu Thr Gln Asn Asp Asn Asp Asn Asp Asn Glu Asp Ala Ala Ala Leu	
7250	7255 7260
ctc cag cag acc ccg tac gcc cag ccc gcc ctc ttc gcc ttc cag gtc	21894
Leu Gln Gln Thr Pro Tyr Ala Gln Pro Ala Leu Phe Ala Phe Gln Val	
7265	7270 7275 7280
gcc ctc cac cgc ctc ctc acc gac ggc tac cac atc acc ccc cac tac	21942
Ala Leu His Arg Leu Leu Thr Asp Gly Tyr His Ile Thr Pro His Tyr	
7285	7290 7295
tac gcc gga cac tcc ctc ggc gaa atc acc gcc gcc cac ctc gcc ggc	21990

Tyr Ala Gly His Ser Leu Gly Glu Ile Thr Ala Ala His Leu Ala Gly
 7300 7305 7310

atc ctc acc ctc acc gac gcc acc acc ctc atc acc caa cgc gcc acc 22038
 Ile Leu Thr Leu Thr Asp Ala Thr Thr Leu Ile Thr Gln Arg Ala Thr
 7315 7320 7325

ctc atg caa acc atg ccc ccc ggc acc atg acc acc ctc cac acc acc 22086
 Leu Met Gln Thr Met Pro Pro Gly Thr Met Thr Thr Leu His Thr Thr
 7330 7335 7340

cca cac cac atc acc cac cac ctc acc gcc cac gaa aac gac ctc gcc 22134
 Pro His His Ile Thr His His Leu Thr Ala His Glu Asn Asp Leu Ala
 7345 7350 7355 7360

atc gcc gcc atc aac acc ccc acc tcc ctc gtc atc agc ggc acc ccc 22182
 Ile Ala Ala Ile Asn Thr Pro Thr Ser Leu Val Ile Ser Gly Thr Pro
 7365 7370 7375

cac acc gtc caa cac atc acc acc ctc tgc caa caa caa ggc atc aaa 22230
 His Thr Val Gln His Ile Thr Thr Leu Cys Gln Gln Gln Gly Ile Lys
 7380 7385 7390

acc aaa acc ctc ccc acc aac cac gcc ttc cac tcc ccc cac acc aac 22278
 Thr Lys Thr Leu Pro Thr Asn His Ala Phe His Ser Pro His Thr Asn
 7395 7400 7405

ccc atc ctc aac caa ctc cac cag cac acc caa acc ctc acc tac cac 22326
 Pro Ile Leu Asn Gln Leu His Gln His Thr Gln Thr Leu Thr Tyr His
 7410 7415 7420

cca ccc cac acc ccc ctc atc acc gcc aac acc cca ccc gac caa ctc 22374
 Pro Pro His Thr Pro Leu Ile Thr Ala Asn Thr Pro Pro Asp Gln Leu
 7425 7430 7435 7440

ctc acc ccc cac tac tgg acc caa caa gcc cgc aac acc gtc gac tac 22422
 Leu Thr Pro His Tyr Trp Thr Gln Gln Ala Arg Asn Thr Val Asp Tyr
 7445 7450 7455

gcc acc acc acc caa acc ctc cac caa cac ggc gtc acc acc tac atc 22470
 Ala Thr Thr Thr Gln Thr Leu His Gln His Gly Val Thr Thr Tyr Ile
 7460 7465 7470

gaa ctc gga ccc gac aac acc ctc acc acc ctc acc cac cac aac ctc 22518
 Glu Leu Gly Pro Asp Asn Thr Leu Thr Thr Leu Thr His His Asn Leu
 7475 7480 7485

ccc aac acc ccc acc acc acc ctc acc ctc acc cac ccc cac cac cac 22566
 Pro Asn Thr Pro Thr Thr Thr Leu Thr Leu Thr His Pro His His His
 7490 7495 7500

ccc caa acc cac ctc ctc acc aac ctc gcc aaa acc acc acc acc tgg 22614
 Pro Gln Thr His Leu Leu Thr Asn Leu Ala Lys Thr Thr Thr Thr Trp
 7505 7510 7515 7520

cac ccc cac cac tac acc cac cac cac aac caa ccc cac acc cac acc 22662
 His Pro His His Tyr Thr His His His Asn Gln Pro His Thr His Thr
 7525 7530 7535

cac ctc gac ctc ccc acc tac ccc ttc caa cac cac cac tac tgg ctc 22710
 His Leu Asp Leu Pro Thr Tyr Pro Phe Gln His His His Tyr Trp Leu
 7540 7545 7550

gaa cta ccc agc gcc caa acc agc ccc ggt caa agg cgt tct cgc cgc 22758
 Glu Leu Pro Ser Ala Gln Thr Ser Pro Gly Gln Arg Arg Ser Arg Arg
 7555 7560 7565

tcg gct cca gac acc gcc gag tcg gag ttc tgg gac gcg gtg aac gag 22806
 Ser Ala Pro Asp Thr Ala Glu Ser Glu Phe Trp Asp Ala Val Asn Glu
 7570 7575 7580

gaa gac ctc cag agc ctc gcc gaa acc ctc gac atc gac gcc tct gct 22854
 Glu Asp Leu Gln Ser Leu Ala Glu Thr Leu Asp Ile Asp Ala Ser Ala
 7585 7590 7595 7600

ctg gac acg gtg gtg ccc gca ctc tcc gcc tgg cac cgc cac caa cac 22902

09914285 002404

Leu Asp Thr Val Val Pro Ala Leu Ser Ala Trp His Arg His Gln His
7605 7610 7615

gac caa gcc cgc atc aac acc tgg acc tac cag gaa acc tgg aaa ccc 22950
Asp Gln Ala Arg Ile Asn Thr Trp Thr Tyr Gln Glu Thr Trp Lys Pro
7620 7625 7630

ctc acc ctc ccc acc acc cac caa ccc cac caa acc tgg ctc atc gcc 22998
Leu Thr Leu Pro Thr Thr His Gln Pro His Gln Thr Trp Leu Ile Ala
7635 7640 7645

atc ccc gaa acc cag acc cac cac ccc cac atc acc aac atc ctc acc 23046
Ile Pro Glu Thr Gln Thr His His Pro His Ile Thr Asn Ile Leu Thr
7650 7655 7660

aac ctc cac cac cac ggc atc acc ccc atc ccc ctc act gtc aac cac 23094
Asn Leu His His His Gly Ile Thr Pro Ile Pro Leu Thr Val Asn His
7665 7670 7675 7680

acc cac acc aac ccc caa cac ctc cac cac acc ctc cac cac acc cga 23142
Thr His Thr Asn Pro Gln His Leu His His Thr Leu His His Thr Arg
7685 7690 7695

caa caa gcc caa aac cac acc acc gga ccc atc acc ggc ctg ctc tcc 23190
Gln Gln Ala Gln Asn His Thr Thr Gly Pro Ile Thr Gly Leu Leu Ser
7700 7705 7710

ctc ctc gcc ctc gac gaa aca ccc cac ccc cac cac ccc cac aca ccc 23238
Leu Leu Ala Leu Asp Glu Thr Pro His Pro His His Pro His Thr Pro
7715 7720 7725

acc ggc acc ctc ctc aac ctc acc ctc ccc caa acc cac acc caa acc 23286
Thr Gly Thr Leu Leu Asn Leu Thr Leu Pro Gln Thr His Thr Gln Thr
7730 7735 7740

cac cca cca acc ccc ctc tgg tac gcc acc acc aac gcc acc acc acc 23334
His Pro Pro Thr Pro Leu Trp Tyr Ala Thr Thr Asn Ala Thr Thr Thr
7745 7750 7755 7760

09914386 032401

cac ccc aac gac ccc ctc aca cac ccc acc caa gcc caa acc tgg gga	23382
His Pro Asn Asp Pro Leu Thr His Pro Thr Gln Ala Gln Thr Trp Gly	
7765 7770 7775	
ctc gcc cgc acc acc ctc ctc gaa cac ccc acc cac acc gcc gga atc	23430
Leu Ala Arg Thr Thr Leu Leu Glu His Pro Thr His Thr Ala Gly Ile	
7780 7785 7790	
atc gac ctc ccc acc acc ccc acc ccc cac acc ctc cac cac ctc acc	23478
Ile Asp Leu Pro Thr Thr Pro Thr Pro His Thr Leu His His Leu Thr	
7795 7800 7805	
caa acc ctc acc caa ccc cac cac caa acc caa ctc gcc atc cgc acc	23526
Gln Thr Leu Thr Gln Pro His His Gln Thr Gln Leu Ala Ile Arg Thr	
7810 7815 7820	
acc ggc acc cac acc cgc cgc ctc acc ccc acc acc ctc acc ccc aca	23574
Thr Gly Thr His Thr Arg Arg Leu Thr Pro Thr Thr Leu Thr Pro Thr	
7825 7830 7835 7840	
cac caa cca ccc acc ccc acc ccc cac gga acc acc ctc atc acc ggc	23622
His Gln Pro Pro Thr Pro Thr Pro His Gly Thr Thr Leu Ile Thr Gly	
7845 7850 7855	
gga acc ggc gcc ctc gcc acc cac ctc acc cac cac ctc acc acc cac	23670
Gly Thr Gly Ala Leu Ala Thr His Leu Thr His His Leu Thr Thr His	
7860 7865 7870	
caa ccc acc caa cac ctc ctc ctc acc agc cga acc ggc ccc cac acc	23718
Gln Pro Thr Gln His Leu Leu Leu Thr Ser Arg Thr Gly Pro His Thr	
7875 7880 7885	
ccc cac gca caa cac ctc acc acc caa ctc caa caa aaa ggc atc cac	23766
Pro His Ala Gln His Leu Thr Thr Gln Leu Gln Gln Lys Gly Ile His	
7890 7895 7900	
ctc acc atc acc acc tgc gac acc agc aac cca gac caa ctc caa caa	23814

gcg cag cgg ccg aat tcc aac ctg atc atc gcg gac atc gac tgg gag 24294
 Ala Gln Arg Pro Asn Ser Asn Leu Ile Ile Ala Asp Ile Asp Trp Glu
 8065 8070 8075 8080

cgc ttc gtc ccc gcc ttc acc gct cga cgc cac agc ccg ctc atc gag 24342
 Arg Phe Val Pro Ala Phe Thr Ala Arg Arg His Ser Pro Leu Ile Glu
 8085 8090 8095

gac att ccg gag gtt cgg caa gcg gct cag gag ctg gaa gca gct gcg 24390
 Asp Ile Pro Glu Val Arg Gln Ala Ala Gln Glu Leu Glu Ala Ala Ala
 8100 8105 8110

tcg acg gca aag acg acc aca gct cag ccg att gcg acg tct ctc cgt 24438
 Ser Thr Ala Lys Thr Thr Thr Ala Gln Pro Ile Ala Thr Ser Leu Arg
 8115 8120 8125

gag cga ttg gcc cga ctg acg tcc tca aag cag aac cag gtg ctg ctc 24486
 Glu Arg Leu Ala Arg Leu Thr Ser Ser Lys Gln Asn Gln Val Leu Leu
 8130 8135 8140

ggc ctg att cgg aca ggc atc tgc acc gtt ctc ggc ctt cgt aat ccg 24534
 Gly Leu Ile Arg Thr Gly Ile Cys Thr Val Leu Gly Leu Arg Asn Pro
 8145 8150 8155 8160

gaa ggc atc gag gac caa cga gcc ttc cgc gac ctc ggc ttc gac tcg 24582
 Glu Gly Ile Glu Asp Gln Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser
 8165 8170 8175

ctg acg tcg gct cag ttc agc aag gaa ctc gcc aag gaa acc gga ctg 24630
 Leu Thr Ser Ala Gln Phe Ser Lys Glu Leu Ala Lys Glu Thr Gly Leu
 8180 8185 8190

cca ctc ccc ccg tcc ctg gtc ttc gac tat ccc acc ccg cag gaa tgt 24678
 Pro Leu Pro Pro Ser Leu Val Phe Asp Tyr Pro Thr Pro Gln Glu Cys
 8195 8200 8205

gct gcc cat ctg cgc aca caa ctc gtc gac cta gac gac gaa gag gac 24726

Ala Ala His Leu Arg Thr Gln Leu Val Asp Leu Asp Asp Glu Glu Asp
 8210 8215 8220

gcg gca ctg tgc aat gct ctc ccg caa gtg gcc cat cgg cgt acc gtc 24774
 Ala Ala Leu Ser Asn Ala Leu Pro Gln Val Ala His Arg Arg Thr Val
 8225 8230 8235 8240

gag gac gaa ccg atc gcc atc atc ggt atg gca tgt cgc ttc ccc ggc 24822
 Glu Asp Glu Pro Ile Ala Ile Ile Gly Met Ala Cys Arg Phe Pro Gly
 8245 8250 8255

ggc gta cgt tct gcc gac gac ctg tgg gaa ttg ctc gct tgc ggt aag 24870
 Gly Val Arg Ser Ala Asp Asp Leu Trp Glu Leu Leu Ala Ser Gly Lys
 8260 8265 8270

gac gct atc ggc gtc ttc ccg acc gac cgc ggc tgg gac ctg gac acg 24918
 Asp Ala Ile Gly Val Phe Pro Thr Asp Arg Gly Trp Asp Leu Asp Thr
 8275 8280 8285

ctc tac gac ccc gac ccc gac cac ccc ggc acc tgc tac acc cga aac 24966
 Leu Tyr Asp Pro Asp Pro Asp His Pro Gly Thr Cys Tyr Thr Arg Asn
 8290 8295 8300

ggc gga ttc ctc tac ggc gca ggc cac ttc gac gcc gaa ttc ttc ggc 25014
 Gly Gly Phe Leu Tyr Gly Ala Gly His Phe Asp Ala Glu Phe Phe Gly
 8305 8310 8315 8320

atc agc ccc cgc gaa gcc ctc gcc atg gac ccc cag caa cga ctc ctc 25062
 Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu
 8325 8330 8335

ctc gaa acc gcc tgg gaa acc atc gaa cac gcc ggc atc aac ccc cac 25110
 Leu Glu Thr Ala Trp Glu Thr Ile Glu His Ala Gly Ile Asn Pro His
 8340 8345 8350

acc ctc cac ggc acc ccc acc gga gtc ttc gcc gga atc aac gct caa 25158
 Thr Leu His Gly Thr Pro Thr Gly Val Phe Ala Gly Ile Asn Ala Gln
 8355 8360 8365

09014286-002401

gac cac gcc gcg cat atc cgc caa agc cgt gat gtg gag acc atc gag 25206
 Asp His Ala Ala His Ile Arg Gln Ser Arg Asp Val Glu Thr Ile Glu
 8370 8375 8380

ggc tac gcc ctg acc ggc agt tcg gga agt gtg gcg tcc ggc cgg gtg 25254
 Gly Tyr Ala Leu Thr Gly Ser Ser Gly Ser Val Ala Ser Gly Arg Val
 8385 8390 8395 8400

gcc tac acg ctc ggg ctc gaa ggc ccc gcg gtg tcg gtg gat acg gcg 25302
 Ala Tyr Thr Leu Gly Leu Glu Gly Pro Ala Val Ser Val Asp Thr Ala
 8405 8410 8415

tgt tcg tcg tcg ttg gtg gcg ttg cat tgg gcg gcg cag gcg ttg cgt 25350
 Cys Ser Ser Ser Leu Val Ala Leu His Trp Ala Ala Gln Ala Leu Arg
 8420 8425 8430

gcg ggt gag tgt tcg atg gcg ctt gcc ggg ggt gtg acg gtg atg tcg 25398
 Ala Gly Glu Cys Ser Met Ala Leu Ala Gly Gly Val Thr Val Met Ser
 8435 8440 8445

tct ccg ggt acg ttt gtg gag ttc tca cgt cag cgg ggt ctg gcc gcg 25446
 Ser Pro Gly Thr Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala
 8450 8455 8460

gac ggg cgg tgc aag gcc tat tcg gcg gct gct gac ggt acc ggc tgg 25494
 Asp Gly Arg Cys Lys Ala Tyr Ser Ala Ala Ala Asp Gly Thr Gly Trp
 8465 8470 8475 8480

gcc gag ggt gtg ggg atg ctg ctg gtg gag cgg ctc tcc gac gcc cgt 25542
 Ala Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Arg
 8485 8490 8495

cgc aac ggt cac cgt gtc ctg gcc gtg gtg cgt ggc agt gcg gtc aac 25590
 Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn
 8500 8505 8510

cag gac ggt gcg agc aac ggt ctg acc gcg ccc aac ggg ccc tcc cag 25638

Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln
 8515 8520 8525

cag cgt gtc atc cgt cag gcc ctg gcc aat gcg gga ctg acc ccg gcc 25686
 Gln Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Thr Pro Ala
 8530 8535 8540

gat gtc gac gca gtg gag ggc cac ggc acc ggg acc act ctg ggg gac 25734
 Asp Val Asp Ala Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly Asp
 8545 8550 8555 8560

ccg atc gag gcc cag gca ctc ctg gcc gcc tac gga caa cac cgc ccc 25782
 Pro Ile Glu Ala Gln Ala Leu Leu Ala Ala Tyr Gly Gln His Arg Pro
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Asp Leu Leu Asn Val Arg Arg Arg Leu Gln Gln Ile Glu Ser Gly Glu
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Gln Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Phe Pro Gly Gly
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385	390	395	400
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Val Leu Pro Arg Thr Leu His Val Asp Glu Pro Ser Ser Gln Val Asp			
405	410	415	
tgg tcg agt ggg tcg gtt cgt gtg ttg gcg gat gag gtg gag tgg ccg			1296
Trp Ser Ser Gly Ser Val Arg Val Leu Ala Asp Glu Val Glu Trp Pro			
420	425	430	
ggg gtg gag ggt cgg ctg cgg cgt gcg ggg gtg tct gcg ttc ggg gtg			1344
Gly Val Glu Gly Arg Leu Arg Arg Ala Gly Val Ser Ala Phe Gly Val			
435	440	445	
agt ggg acg aat gcg cat gtg att ttg gag gag gcg tcg ggg ggc gcg			1392
Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu Ala Ser Gly Gly Ala			
450	455	460	
ggt ggg ggt gcg ggc cgg ctg cag gag ttg ggt ccg ggg gtg gtg tcg			1440
Gly Gly Gly Ala Gly Arg Leu Gln Glu Leu Gly Pro Gly Val Val Ser			
465	470	475	480
ggt tcg ggg gtg gtg ccg tgg gtg gtg tcg gcg cgg tcg gag ttg gcg			1488
Gly Ser Gly Val Val Pro Trp Val Val Ser Ala Arg Ser Glu Leu Ala			
485	490	495	
ttg cgg ggg cag gcg cgt cgg ttg cgt ggg gtt gtg gcg gtt ggt ggg			1536
Leu Arg Gly Gln Ala Arg Arg Leu Arg Gly Val Val Ala Val Gly Gly			
500	505	510	

ggt gcg gat ggt gtg ggg gtg agt ccg gct ggg gtc ggg cgg gct ttg 1584
 Gly Ala Asp Gly Val Gly Val Ser Pro Ala Gly Val Gly Arg Ala Leu
 515 520 525

gtg tcg gag cgg tcg gtg ttc gag cat cgt gcg gtg gtc gtg gcc gag 1632
 Val Ser Glu Arg Ser Val Phe Glu His Arg Ala Val Val Val Ala Glu
 530 535 540

gac cgc gac gag ttc ctg cac gca ctc gac gca ctg gcc ggc ggc cgc 1680
 Asp Arg Asp Glu Phe Leu His Ala Leu Asp Ala Leu Ala Gly Gly Arg
 545 550 555 560

ccc gtg ccc ggc gtc gtc gag gga cga acc acc tcg ggc gaa ctc gcc 1728
 Pro Val Pro Gly Val Val Glu Gly Arg Thr Thr Ser Gly Glu Leu Ala
 565 570 575

gta ctc ttc gcc ggg cag gga acc cag cgc gca ggc atg ggc cgc gaa 1776
 Val Leu Phe Ala Gly Gln Gly Thr Gln Arg Ala Gly Met Gly Arg Glu
 580 585 590

ctg tac gag gcg tac ccc gtc ttc gcc cag gcc atc gac gag atc tgc 1824
 Leu Tyr Glu Ala Tyr Pro Val Phe Ala Gln Ala Ile Asp Glu Ile Cys
 595 600 605

gcg gag gcc gac acc gcc cgc acc gac ccc ggt gcc cct ggg ctg cgg 1872
 Ala Glu Ala Asp Thr Ala Arg Thr Asp Pro Gly Ala Pro Gly Leu Arg
 610 615 620

gac gta ctc ttc gca ccg cag gac tct ccc gaa ggc cgg ctg atc gag 1920
 Asp Val Leu Phe Ala Pro Gln Asp Ser Pro Glu Gly Arg Leu Ile Glu
 625 630 635 640

gac acg ggt ttc gcc cag ccc gcc ctg ttc gcc ttc gag gtg gcg ctg 1968
 Asp Thr Gly Phe Ala Gln Pro Ala Leu Phe Ala Phe Glu Val Ala Leu
 645 650 655

ttc cgg ctg ctg gag acc tgg ggt ctg acg ccc gac tac gtc ctc ggc 2016
 Phe Arg Leu Leu Glu Thr Trp Gly Leu Thr Pro Asp Tyr Val Leu Gly

660	665	670	
cat tcc gtc ggt gaa ctg gcg gcc gcc cat gtc gcc ggg atg ctc tgc	2064		
His Ser Val Gly Glu Leu Ala Ala Ala His Val Ala Gly Met Leu Cys			
675	680	685	
ctt gcc gac gcg gtg gca ctg gtg gtc gca cga ggc cgc ctg atg caa	2112		
Leu Ala Asp Ala Val Ala Leu Val Val Ala Arg Gly Arg Leu Met Gln			
690	695	700	
ggg ctc ccg tcc ggc gga gcc atg gtg gcc atc gag gcg tcc gag gac	2160		
Gly Leu Pro Ser Gly Gly Ala Met Val Ala Ile Glu Ala Ser Glu Asp			
705	710	715	720
gag atc ctc ccg ctg ccc gac gaa tac gca tcc cgg gtc gcg cac gcc	2208		
Glu Ile Leu Pro Leu Pro Asp Glu Tyr Ala Ser Arg Val Ala His Ala			
725	730	735	
gcg gtg aac ggg ccg cgg tcg atc gtc ctc tcc ggg gac gag gac gcg	2256		
Ala Val Asn Gly Pro Arg Ser Ile Val Leu Ser Gly Asp Glu Asp Ala			
740	745	750	
gtc ctg gac ctc gcg cag caa tgg gcg gca cga ggc cgc cgc acc cgg	2304		
Val Leu Asp Leu Ala Gln Gln Trp Ala Ala Arg Gly Arg Arg Thr Arg			
755	760	765	
cgg ctg cgg acc agc cac gcc ttc cac tcg ccg cac atg gac gcc atg	2352		
Arg Leu Arg Thr Ser His Ala Phe His Ser Pro His Met Asp Ala Met			
770	775	780	
ttg ggc gac ttc cgc cgc gcg gcc gag cag gtc acc ttc agc gcc ccg	2400		
Leu Gly Asp Phe Arg Arg Ala Ala Glu Gln Val Thr Phe Ser Ala Pro			
785	790	795	800
cgg att ccc gtc gtc tcc aac gtc acc ggc gcg ccc ctc ccc gcc gag	2448		
Arg Ile Pro Val Val Ser Asn Val Thr Gly Ala Pro Leu Pro Ala Glu			
805	810	815	

acc atg tgc acc ccg gac tac tgg gtc gaa cac gcc cgc agc acg gtc 2496
 Thr Met Cys Thr Pro Asp Tyr Trp Val Glu His Ala Arg Ser Thr Val
 820 825 830

cgt ttc gcg gac ggc atc tca tgg ctt cag gaa cag ggc gtc acc acc 2544
 Arg Phe Ala Asp Gly Ile Ser Trp Leu Gln Glu Gln Gly Val Thr Thr
 835 840 845

tgc ctc gaa atc ggc ccc gac ggc acg ctg tcg gcc ctc gca cag gac 2592
 Cys Leu Glu Ile Gly Pro Asp Gly Thr Leu Ser Ala Leu Ala Gln Asp
 850 855 860

tcg ctc agt gca ccg gcc cgc gcc atc ccc gcc ctg cgg ccg gac cag 2640
 Ser Leu Ser Ala Pro Ala Arg Ala Ile Pro Ala Leu Arg Pro Asp Gln
 865 870 875 880

ccg gag gca cgg tcg gtc atg acc gcc ctg gcg gag ttg ttc gtg gct 2688
 Pro Glu Ala Arg Ser Val Met Thr Ala Leu Ala Glu Leu Phe Val Ala
 885 890 895

ggg acg gcg gtt gag tgg gcc ggt gtg ttc gag ggg act gct cgc gag 2736
 Gly Thr Ala Val Glu Trp Ala Gly Val Phe Glu Gly Thr Ala Arg Glu
 900 905 910

gtc ggt gat gga tgc ggg gtg gag ctg ccg acg tat gcg ttt gag cgg 2784
 Val Gly Asp Gly Cys Gly Val Glu Leu Pro Thr Tyr Ala Phe Glu Arg
 915 920 925

gag cga ttt tgg ctg gac gtg gag gag gga tct gcg gga ggt tcc ggg 2832
 Glu Arg Phe Trp Leu Asp Val Glu Glu Gly Ser Ala Gly Gly Ser Gly
 930 935 940

gtt tcc ggg atg tgg ggt ggt ccg ttg tgg gag gcg gtc gag tgt ggt 2880
 Val Ser Gly Met Trp Gly Gly Pro Leu Trp Glu Ala Val Glu Cys Gly
 945 950 955 960

gat gcg ggg gtg gtg gca tcg ctc ctt ggg gtg gat gag ggg gcg tcg 2928
 Asp Ala Gly Val Val Ala Ser Leu Leu Gly Val Asp Glu Gly Ala Ser

00914335-082404
T04280-9824T660

965

970

975

ctg ggt gcg gtg gtg tgc gcg ttg ggg gaa tgg ggg cgg gta cgg cac 2976
Leu Gly Ala Val Val Ser Ala Leu Gly Glu Trp Gly Arg Val Arg His
980 985 990

gag cgt gaa gtg gtg gac ggg tgg cgc tat cgg gag gtg tgg cga ccc 3024
Glu Arg Glu Val Val Asp Gly Trp Arg Tyr Arg Glu Val Trp Arg Pro
995 1000 1005

gtt tgc ggc ggt ggt gta ggg ggg ctg tgc ggc gcg tgg ctg gtg gtg 3072
Val Ser Gly Gly Gly Val Gly Gly Leu Ser Gly Ala Trp Leu Val Val
1010 1015 1020

tcc gag ggc gag gcg ggc ccg gtt gat gtg gtg gcg gag ggg ttg gag 3120
Ser Glu Gly Glu Ala Gly Pro Val Asp Val Val Ala Glu Gly Leu Glu
1025 1030 1035 1040

cgg tgt ggg gcg cga gtg gtt cgg gtg gag gtg gaa gcg ggg tgt gtg 3168
Arg Cys Gly Ala Arg Val Val Arg Val Glu Val Glu Ala Gly Cys Val
1045 1050 1055

agc agg gaa gtg ttg gcc ggc cac ctg cgt gag gcg gtc gat ggt gag 3216
Ser Arg Glu Val Leu Ala Gly His Leu Arg Glu Ala Val Asp Gly Glu
1060 1065 1070

gct gtc ggc ggt gtc gtc tcc ctt gtg ggc tgg ggg agt ggc gtc gtg 3264
Ala Val Gly Gly Val Val Ser Leu Val Gly Trp Gly Ser Gly Val Val
1075 1080 1085

cag gcg gga gtg gcg tct gtg ggg ttg gtg cag gcg ctg ggt gat gtg 3312
Gln Ala Gly Val Ala Ser Val Gly Leu Val Gln Ala Leu Gly Asp Val
1090 1095 1100

ggc gtg ggg gcg cgg ctg tgg tgt gtg acg ggc ggg gcc gtg tgc gtg 3360
Gly Val Gly Ala Arg Leu Trp Cys Val Thr Gly Gly Ala Val Ser Val
1105 1110 1115 1120

05914286 002491

1265	1270	1275	1280
gag gtg ttg cgg tcg gcc gtt ccg gcg gag tgc ccg ctg ggt gtg gtg 3888			
Glu Val Leu Arg Ser Ala Val Pro Ala Glu Cys Pro Leu Gly Val Val			
1285	1290	1295	
gtg cat gcc gcg gga gtt gtg gat gac ggg gtg ttg gag ggg ttg tcg 3936			
Val His Ala Ala Gly Val Val Asp Asp Gly Val Leu Glu Gly Leu Ser			
1300	1305	1310	
tcc gag cgt gtc acg ggg gtg ctg cgg gcg aag gcg ctg gcg gcc tgg 3984			
Ser Glu Arg Val Thr Gly Val Leu Arg Ala Lys Ala Leu Ala Ala Trp			
1315	1320	1325	
aat ctg cat gag ttg acg cgg ggg gcg gat ctt tcg ggg ttc gtg gtg 4032			
Asn Leu His Glu Leu Thr Arg Gly Ala Asp Leu Ser Gly Phe Val Val			
1330	1335	1340	
ttc tcg tcg gct gcg gcg acg ttc ggg ccg gcg gga cag ggg agt tac 4080			
Phe Ser Ser Ala Ala Ala Thr Phe Gly Pro Ala Gly Gln Gly Ser Tyr			
1345	1350	1355	1360
gcg gcg gcg aac gcg tat gtg gag gca atc gtt cgg cac cgg cgt ggt 4128			
Ala Ala Ala Asn Ala Tyr Val Glu Ala Ile Val Arg His Arg Arg Gly			
1365	1370	1375	
gag ggc ctg ccg ggg ttg gcg gtg gcg tgg ggt ccg tgg gct ggt ggg 4176			
Glu Gly Leu Pro Gly Leu Ala Val Ala Trp Gly Pro Trp Ala Gly Gly			
1380	1385	1390	
ggg atg gcg gag ggg gcc gtg ggg cag atg ccg cgt ccg ggt ctg gcg 4224			
Gly Met Ala Glu Gly Ala Val Gly Gln Met Arg Arg Arg Gly Leu Ala			
1395	1400	1405	
gcg atg acg ccg gag acg gcg ctg gtg gca ctg ggc cag gcg ttg gac 4272			
Ala Met Thr Pro Glu Thr Ala Leu Val Ala Leu Gly Gln Ala Leu Asp			
1410	1415	1420	

cat gac gag acc tgt gtg acg gtc gcc gac atc gac tgg gac cga ttc 4320
 His Asp Glu Thr Cys Val Thr Val Ala Asp Ile Asp Trp Asp Arg Phe
 1425 1430 1435 1440

acc gcc aac tcc ctc ccc ggc tcc cga ctc tcg ccc ctc atc agc gac 4368
 Thr Ala Asn Ser Leu Pro Gly Ser Arg Leu Ser Pro Leu Ile Ser Asp
 1445 1450 1455

atc ccc gaa gca cgc ctc gcc cgg gaa acc acc gga ctc gac acc gcc 4416
 Ile Pro Glu Ala Arg Leu Ala Arg Glu Thr Thr Gly Leu Asp Thr Ala
 1460 1465 1470

acc gca tcc ccc gac tcg ttc tcc gca cgg ctc aag gcc atg gac acc 4464
 Thr Ala Ser Pro Asp Ser Phe Ser Ala Arg Leu Lys Ala Met Asp Thr
 1475 1480 1485

gcc gag cag gaa cgt gcg ctt ctc gac ctg gtc cgt acg tac gcg gcg 4512
 Ala Glu Gln Glu Arg Ala Leu Leu Asp Leu Val Arg Thr Tyr Ala Ala
 1490 1495 1500

acc gtg ctc gga cac agc acc ccc acc gcc gta cgc cct gag cga gcc 4560
 Thr Val Leu Gly His Ser Thr Pro Thr Ala Val Arg Pro Glu Arg Ala
 1505 1510 1515 1520

ttc cgc gac ctg ggc ttc gtc tcc gtg agc gcc gtc gaa ctg cgc aac 4608
 Phe Arg Asp Leu Gly Phe Val Ser Val Ser Ala Val Glu Leu Arg Asn
 1525 1530 1535

cgc ctc aac gcc gtc acc ggg ctc ctc ctg ccc acc acg ctg atc ttc 4656
 Arg Leu Asn Ala Val Thr Gly Leu Leu Leu Pro Thr Thr Leu Ile Phe
 1540 1545 1550

gac tac ccc act ccc tcc gcg ctg gcc gga tac ctc aag gaa cag ctg 4704
 Asp Tyr Pro Thr Pro Ser Ala Leu Ala Gly Tyr Leu Lys Glu Gln Leu
 1555 1560 1565

gag gag ggc gcg ggc ggc cag cgt gac att gct cct ccg gtc ccg gcg 4752
 Glu Glu Gly Ala Gly Gly Gln Arg Asp Ile Ala Pro Pro Val Pro Ala

09914936-000401

1570	1575	1580	
tcg cgt gtc gac gtt gac gag ccg att gcg att gtg ggg atg gcg tgc			4800
Ser Arg Val Asp Val Asp Glu Pro Ile Ala Ile Val Gly Met Ala Cys			
1585	1590	1595	1600
cg1 ttt ccg ggg ggt gtg gag tcg gcg gag gac ttg tgg gaa ctg gtc			4848
Arg Phe Pro Gly Gly Val Glu Ser Ala Glu Asp Leu Trp Glu Leu Val			
1605	1610	1615	
gcg tcg ggt cgg gat gcg gtg gga gag ttt ccg gtc gac cgg ggt tgg			4896
Ala Ser Gly Arg Asp Ala Val Gly Glu Phe Pro Val Asp Arg Gly Trp			
1620	1625	1630	
gac gtg gag gct ttc tat gat ccg gag ccg ggg cgg gcg ggt tcg tcg			4944
Asp Val Glu Ala Phe Tyr Asp Pro Glu Pro Gly Arg Ala Gly Ser Ser			
1635	1640	1645	
tat acg cgc cgg ggc ggt ttc ctg gag ggt gcg gcg gag ttc gat gcg			4992
Tyr Thr Arg Arg Gly Gly Phe Leu Glu Gly Ala Ala Glu Phe Asp Ala			
1650	1655	1660	
ggg ttt ttc ggg atc agt ccg cgt gag gcg ttg gcg atg gat ccg cag			5040
Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln			
1665	1670	1675	1680
cag cgg ttg atg ctg gag gtg tcc tgg gag gcg ttg gag cgg gcg ggc			5088
Gln Arg Leu Met Leu Glu Val Ser Trp Glu Ala Leu Glu Arg Ala Gly			
1685	1690	1695	
atc gac ccc gcc acg ttg cgc ggg tcc acg acc ggt gtc ttc gcc ggc			5136
Ile Asp Pro Ala Thr Leu Arg Gly Ser Thr Thr Gly Val Phe Ala Gly			
1700	1705	1710	
atg tgc agt cag gac tac gcc gac ctc gtg cgc cgg gcc acc gag gac			5184
Met Cys Ser Gln Asp Tyr Ala Asp Leu Val Arg Arg Ala Thr Glu Asp			
1715	1720	1725	

ctc gag ggc tac gcc atg acg ggc ctg tcc agc agc gtc aca tcc gga 5232
 Leu Glu Gly Tyr Ala Met Thr Gly Leu Ser Ser Ser Val Thr Ser Gly
 1730 1735 1740

cgc gtc gcc tac acc ctg ggg ctc gag ggt ccg gcg gtg acg gtg gat 5280
 Arg Val Ala Tyr Thr Leu Gly Leu Glu Gly Pro Ala Val Thr Val Asp
 1745 1750 1755 1760

acg gcg tgt tcg tcg tcg ttg gtg gcg ctg cat ctg gcg tgt cag gcg 5328
 Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala
 1765 1770 1775

ttg agg tcg ggg gag tgt tcg ctg gcg ttg gcg ggg ggt gtg acg gtg 5376
 Leu Arg Ser Gly Glu Cys Ser Leu Ala Leu Ala Gly Gly Val Thr Val
 1780 1785 1790

atg tcg acg ccg ggt gcg ttt gtg gag ttc tcg cgg cag cgg ggt ctg 5424
 Met Ser Thr Pro Gly Ala Phe Val Glu Phe Ser Arg Gln Arg Gly Leu
 1795 1800 1805

tcg ccg gac ggc cgg tgc aag gcg tac ggg tcg ggg gcc gat ggg gtc 5472
 Ser Pro Asp Gly Arg Cys Lys Ala Tyr Gly Ser Gly Ala Asp Gly Val
 1810 1815 1820

ggc tgg gcc gag ggt gtg ggt gtg ctg ttg gtg gag cgg ctg tcc gag 5520
 Gly Trp Ala Glu Gly Val Gly Val Leu Leu Val Glu Arg Leu Ser Glu
 1825 1830 1835 1840

gct gaa cgt cgt ggt cat cgg gtt ttg gcg gtg gtg cgg ggg agt gcg 5568
 Ala Glu Arg Arg Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala
 1845 1850 1855

gtg aat cag gac ggt gcg tcg aat ggg ttg acg gcg ccg aat ggt ccg 5616
 Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro
 1860 1865 1870

tcg cag cag cgg gtg att cgg cag gcg ttg gcg tgt gcg ggg ttg tcc 5664
 Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Cys Ala Gly Leu Ser

1875

1880

1885

gtg gcg gat gtg gat gtg gtg gag ggg cac ggg acg ggt acg acg ttg 5712
Val Ala Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr Thr Leu

1890

1895

1900

ggt gat ccg atc gag gcg cag gcg ttg ctc gcc act tat ggg cag ggt 5760
Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Gly

1905

1910

1915

1920

cgt tcg ggg gag cgg ccg gtg tgg ttg ggg tcg gtg aag tcg aac atc 5808
Arg Ser Gly Glu Arg Pro Val Trp Leu Gly Ser Val Lys Ser Asn Ile

1925

1930

1935

ggg cat gcg cag gct gct gcg ggt gtg gcg ggt gtg atc aag atg gtg 5856
Gly His Ala Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val

1940

1945

1950

atg gcg ttg cgg gcg ggg gtg ttg ccg cgg acg ttg cat gtg gat gag 5904
Met Ala Leu Arg Ala Gly Val Leu Pro Arg Thr Leu His Val Asp Glu

1955

1960

1965

ccg tcg tcg cag gtg gat tgg tcg agt ggg tcg gtt cgt gtg ttg gcg 5952
Pro Ser Ser Gln Val Asp Trp Ser Ser Gly Ser Val Arg Val Leu Ala

1970

1975

1980

gat gag gtg gag tgg ccg ggg gtg gag ggt cgg ctg cgg cgt gcg ggg 6000
Asp Glu Val Glu Trp Pro Gly Val Glu Gly Arg Leu Arg Arg Ala Gly

1985

1990

1995

2000

gtg tct gcg ttc ggg gtg agt ggg acg aat gcg cat gtg att ttg gag 6048
Val Ser Ala Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu

2005

2010

2015

gag gcg tcc ggg ggc gcg gat ggg ggt gcg ggc cgg ctg cag gag ttg 6096
Glu Ala Ser Gly Gly Ala Asp Gly Gly Ala Gly Arg Leu Gln Glu Leu

2020

2025

2030

ggt ccg ggg gtg gtg tcg ggt tcg ggg gtg gtg ccg tgg gtg gtg tcg 6144
 Gly Pro Gly Val Val Ser Gly Ser Gly Val Val Pro Trp Val Val Ser
 2035 2040 2045

gcg cgg tcg gag ttg gcg ttg cgg ggg cag gcg cgt cgg ttg cgt ggg 6192
 Ala Arg Ser Glu Leu Ala Leu Arg Gly Gln Ala Arg Arg Leu Arg Gly
 2050 2055 2060

gtt gtg gcg gtt ggt ggg ggt gcg gat ggt gtg ggg gtg agt ccg gct 6240
 Val Val Ala Val Gly Gly Gly Ala Asp Gly Val Gly Val Ser Pro Ala
 2065 2070 2075 2080

ggg gtc ggg cgg gct ttg gtg tcg gag cgg tcg gtg ttc gag cat cgt 6288
 Gly Val Gly Arg Ala Leu Val Ser Glu Arg Ser Val Phe Glu His Arg
 2085 2090 2095

gcg gtg gtc gtg gcc gag gac cgc gac gag ttc ctg cac gca ctc gac 6336
 Ala Val Val Val Ala Glu Asp Arg Asp Glu Phe Leu His Ala Leu Asp
 2100 2105 2110

gca ctg gcc gag ggg gca ccc acc gcg ggg gtg gta cag ggt gtg gcc 6384
 Ala Leu Ala Glu Gly Ala Pro Thr Ala Gly Val Val Gln Gly Val Ala
 2115 2120 2125

gga ccg gcg gcc gac gga aag atc gcc atg ctg ttc gga gga cag ggc 6432
 Gly Pro Ala Ala Asp Gly Lys Ile Ala Met Leu Phe Gly Gly Gln Gly
 2130 2135 2140

acc cac tgg gaa ggc atg gcg cag gaa ctc ctc ggc tcc tca ccg gtc 6480
 Thr His Trp Glu Gly Met Ala Gln Glu Leu Leu Gly Ser Ser Pro Val
 2145 2150 2155 2160

ttc gcc cag cag atg tcc gac tgc gcc caa gcc ctc gaa ccg tac ctg 6528
 Phe Ala Gln Gln Met Ser Asp Cys Ala Gln Ala Leu Glu Pro Tyr Leu
 2165 2170 2175

gac tgg tct ctc ctc gac gtc ctg cgc ggc gca ccg gac gca ccc cct 6576
 Asp Trp Ser Leu Leu Asp Val Leu Arg Gly Ala Pro Asp Ala Pro Pro

2180

2185

2190

ctg caa cgc gtc gat gtc gtc cag ccc gtc ctc ttc gcg gtg atg gtc 6624
Leu Gln Arg Val Asp Val Val Gln Pro Val Leu Phe Ala Val Met Val

2195

2200

2205

tcg ctg gcg gcg ctc tgg cgc tcg tac ggt gta cac ccg gac gcg gtg 6672
Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Val His Pro Asp Ala Val

2210

2215

2220

gcc ggg cac tcg cag ggc gag atc gca gcg gcc tac gtc gcc ggt gca 6720
Ala Gly His Ser Gln Gly Glu Ile Ala Ala Ala Tyr Val Ala Gly Ala

2225

2230

2235

2240

ctc tcc ctc gac gac gcc gcc cgg gtc acc gcc ctg cgc agc cag gcg 6768
Leu Ser Leu Asp Asp Ala Ala Arg Val Thr Ala Leu Arg Ser Gln Ala

2245

2250

2255

ctg gcc gca ctg gcc ggg cag ggg gcg atg gca tcg gtc ggt ctg ccg 6816
Leu Ala Ala Leu Ala Gly Gln Gly Ala Met Ala Ser Val Gly Leu Pro

2260

2265

2270

gtc gag aag ctg gag ccg cgt ctt gcg aca tgg ggc gac cgt ctg gtc 6864
Val Glu Lys Leu Glu Pro Arg Leu Ala Thr Trp Gly Asp Arg Leu Val

2275

2280

2285

atc gcc gcc gtg aac ggg gcg cgt tcg gcc gtg gtc tcc ggg gag ccg 6912
Ile Ala Ala Val Asn Gly Ala Arg Ser Ala Val Val Ser Gly Glu Pro

2290

2295

2300

gaa gcg gtc gac gcc ctg gtg gag gag ctg tca cac gaa gac gta ccg 6960
Glu Ala Val Asp Ala Leu Val Glu Glu Leu Ser His Glu Asp Val Pro

2305

2310

2315

2320

gcc cgc agg ctc atg gtc gac tgg gcg tcg cac tcc ccg cag gtc gag 7008
Ala Arg Arg Leu Met Val Asp Trp Ala Ser His Ser Pro Gln Val Glu

2325

2330

2335

gcg atc cag ggg cgg ctg ctc gaa ctc ctc gcc ccc atc cgc gcg agg 7056
 Ala Ile Gln Gly Arg Leu Leu Glu Leu Leu Ala Pro Ile Arg Ala Arg
 2340 2345 2350

acc ggc gac gtg ccc ttc tac tcc acc gtc acc ggc gaa cgc atc gac 7104
 Thr Gly Asp Val Pro Phe Tyr Ser Thr Val Thr Gly Glu Arg Ile Asp
 2355 2360 2365

ggc acc gaa ctc gac gcc gac tac tgg tac cgc aac ctg cgc cag gtc 7152
 Gly Thr Glu Leu Asp Ala Asp Tyr Trp Tyr Arg Asn Leu Arg Gln Val
 2370 2375 2380

gtc cgc ttc cgg gac gcg aca cag gcg ctg gtc cgc gcc ggc cac acc 7200
 Val Arg Phe Arg Asp Ala Thr Gln Ala Leu Val Arg Ala Gly His Thr
 2385 2390 2395 2400

gtc ttc atc gag gcg tgc ccg cat ccg gcc gtc gcg gtc ggt gtg cag 7248
 Val Phe Ile Glu Ala Cys Pro His Pro Ala Val Ala Val Gly Val Gln
 2405 2410 2415

gaa acc ctg gac gag atg ggt gac ttg gac agc ctg gtc gtc gga tct 7296
 Glu Thr Leu Asp Glu Met Gly Asp Leu Asp Ser Leu Val Val Gly Ser
 2420 2425 2430

ctg cgc cgg ggc gaa ggc ggc ttg cga cgc ttc ctg atg tcc gtg gcc 7344
 Leu Arg Arg Gly Glu Gly Gly Leu Arg Arg Phe Leu Met Ser Val Ala
 2435 2440 2445

gag ttg ttc gtg ggt ggg gtg gcg gtt gag tgg tcc ggt gtg ttc ggg 7392
 Glu Leu Phe Val Gly Gly Val Ala Val Glu Trp Ser Gly Val Phe Gly
 2450 2455 2460

agt gtt ggt cgc ggg gtc gct ggt ggt tgc ggg gtg gag ctg ccg acg 7440
 Ser Val Gly Arg Gly Val Ala Gly Gly Cys Gly Val Glu Leu Pro Thr
 2465 2470 2475 2480

tat gcg ttc gag cga gag cgc ttt tgg ctg gat gtg gag ggg gcg ccg 7488
 Tyr Ala Phe Glu Arg Glu Arg Phe Trp Leu Asp Val Glu Gly Ala Pro

2485	2490	2495	
cgg ggt tcc ggg gtc tct ggg cag tgg ggt ggt cag ttg tgc gag gcg	7536		
Arg Gly Ser Gly Val Ser Gly Gln Trp Gly Gly Gln Leu Ser Glu Ala			
2500	2505	2510	
gtg gac acc gtg cgc ggc ggc atg ctg cgc gac tgc ctc gcc gga ctc	7584		
Val Asp Thr Val Arg Gly Gly Met Leu Arg Asp Cys Leu Ala Gly Leu			
2515	2520	2525	
gac ccc gcc gca cag gcc gag acc gtg ctg gac ctg gtc ctt acc cat	7632		
Asp Pro Ala Ala Gln Ala Glu Thr Val Leu Asp Leu Val Leu Thr His			
2530	2535	2540	
gcc gcg gcc gtc ctt gga cac ggc acc gcc gat gcg gtg gtg ccc gag	7680		
Ala Ala Ala Val Leu Gly His Gly Thr Ala Asp Ala Val Val Pro Glu			
2545	2550	2555	2560
cgc gcc ttc cgc gac ctc ggt ttc gac tcc ctc acc gcc gtc gaa cta	7728		
Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu			
2565	2570	2575	
cgc aac cgc ctc aac acc gcc acg ggc ctg cgc ttc ccg agg acc ctg	7776		
Arg Asn Arg Leu Asn Thr Ala Thr Gly Leu Arg Phe Pro Arg Thr Leu			
2580	2585	2590	
gtg ttc gac cat ccc cgc ccg gtg gca ctc gcg gca cac atc cac gag	7824		
Val Phe Asp His Pro Arg Pro Val Ala Leu Ala Ala His Ile His Glu			
2595	2600	2605	
cag ctg agc ggc gga agc ccg acc acc ggc act gcc ctt gcc ctt gcc	7872		
Gln Leu Ser Gly Gly Ser Pro Thr Thr Gly Thr Ala Leu Ala Leu Ala			
2610	2615	2620	
ctt cgg gcc ccg gca ccg cgt gtg gat gtc gac gag ccg att gcc att	7920		
Leu Arg Ala Pro Ala Pro Arg Val Asp Val Asp Glu Pro Ile Ala Ile			
2625	2630	2635	2640

gtg ggg atg gcg tgc cgt ttt ccg ggg ggt gtg gag tcg gcg gag gat 7968
Val Gly Met Ala Cys Arg Phe Pro Gly Gly Val Glu Ser Ala Glu Asp
2645 2650 2655

ttc tgg gag ttg atc gcg tcg ggt cgg gat gcg gtg ggg gag ttt ccg 8016
Phe Trp Glu Leu Ile Ala Ser Gly Arg Asp Ala Val Gly Glu Phe Pro
2660 2665 2670

gtc gac cgg ggt tgg gac gtg gag gct ttc tat gat ccg gag ccg ggg 8064
Val Asp Arg Gly Trp Asp Val Glu Ala Phe Tyr Asp Pro Glu Pro Gly
2675 2680 2685

cgg gcg ggt acg tcc tac acg cgg tgt ggt ggg ttt ttg cag ggt gcg 8112
Arg Ala Gly Thr Ser Tyr Thr Arg Cys Gly Gly Phe Leu Gln Gly Ala
2690 2695 2700

gcg gag ttc gat gcg ggg ttt ttc ggg atc agt ccg cgt gag gcg ttg 8160
Ala Glu Phe Asp Ala Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu
2705 2710 2715 2720

gcg atg gat ccg cag cag cgg ttg atg ctg gag gtg tcc tgg gag gcg 8208
Ala Met Asp Pro Gln Gln Arg Leu Met Leu Glu Val Ser Trp Glu Ala
2725 2730 2735

ttg gag cgg gcg ggc atc gac ccc gcc acg ctg cac ggg tcc acg acc 8256
Leu Glu Arg Ala Gly Ile Asp Pro Ala Thr Leu His Gly Ser Thr Thr
2740 2745 2750

ggt gtc ttc gcc ggc gtc tcg cag cag gac tac gcc gag ctc ctg cgc 8304
Gly Val Phe Ala Gly Val Ser Gln Gln Asp Tyr Ala Glu Leu Leu Arg
2755 2760 2765

cgc ggc acc cag gac cac gag ggg tac gcg ctc acc ggc gtc tcc aac 8352
Arg Gly Thr Gln Asp His Glu Gly Tyr Ala Leu Thr Gly Val Ser Asn
2770 2775 2780

agc gtc gtc tcc ggg cgg ctt tcc tac acc ttc ggc ttc gag ggt ccg 8400
Ser Val Val Ser Gly Arg Leu Ser Tyr Thr Phe Gly Phe Glu Gly Pro

2785

2790

2795

2800

gcg gtg acg gtg gat acg gcg tgt tgc tgc tgc ttg gtg gcg ctg cat 8448

Ala Val Thr Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His

2805

2810

2815

ctg gcg tgt cag gcg ttg agg tgc ggg gag tgt tgc ctg gcg ttg gcg 8496

Leu Ala Cys Gln Ala Leu Arg Ser Gly Glu Cys Ser Leu Ala Leu Ala

2820

2825

2830

ggg ggt gtg acg gtg atg tgc acg ccg ggt gcg ttt gtg gag ttc tgc 8544

Gly Gly Val Thr Val Met Ser Thr Pro Gly Ala Phe Val Glu Phe Ser

2835

2840

2845

cgg cag cgg ggt ctg tgc ccg gac ggc cgg tgc aag gcg tac ggg tgc 8592

Arg Gln Arg Gly Leu Ser Pro Asp Gly Arg Cys Lys Ala Tyr Gly Ser

2850

2855

2860

ggg gcc gat ggg gtc ggc tgg gcc gag ggt gtg ggt gtg ctg ttg gtg 8640

Gly Ala Asp Gly Val Gly Trp Ala Glu Gly Val Gly Val Leu Leu Val

2865

2870

2875

2880

gag cgg ctg tcc gag gct gaa cgt cgt ggt cat cgg gtt ttg gcg gtg 8688

Glu Arg Leu Ser Glu Ala Glu Arg Arg Gly His Arg Val Leu Ala Val

2885

2890

2895

gtg cgg ggg agt gcg gtg aat cag gac ggt gcg tgc aat ggg ttg acg 8736

Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr

2900

2905

2910

gcg ccg aat ggt ccg tgc cag cag cgg gtg att cgg cag gcg ttg gcg 8784

Ala Pro Asn Gly Pro Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala

2915

2920

2925

tgt gcg ggg ttg tcc gtg gcg gat gtg gat gtg gtg gag ggg cac ggg 8832

Cys Ala Gly Leu Ser Val Ala Asp Val Asp Val Val Glu Gly His Gly

2930

2935

2940

F01280-9824T660

acg ggt acg acg ttg ggt gat ccg atc gag gcg cag gcg ttg ctc gcc 8880
 Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala
 2945 2950 2955 2960

acg tac ggg cag ggt cgt tcg ggg gag cgg ccg gtg tgg ttg ggg tcg 8928
 Thr Tyr Gly Gln Gly Arg Ser Gly Glu Arg Pro Val Trp Leu Gly Ser
 2965 2970 2975

gtg aag tcg aac atc ggg cat gcg cag gct gcc gcg ggt gtg gcc ggt 8976
 Val Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala Gly Val Ala Gly
 2980 2985 2990

gtg atc aag atg gtc atg gcc ctg aac cac gaa ctg ttg ccg acc agc 9024
 Val Ile Lys Met Val Met Ala Leu Asn His Glu Leu Leu Pro Thr Ser
 2995 3000 3005

ctg cac atc gac gaa ccc tcc ccc cac atc gac tgg tcg agc ggc ggc 9072
 Leu His Ile Asp Glu Pro Ser Pro His Ile Asp Trp Ser Ser Gly Gly
 3010 3015 3020

gtc cgg ctt ctc acc gag ccc gta ccg tgg cag cag aac ggc cgg ccc 9120
 Val Arg Leu Leu Thr Glu Pro Val Pro Trp Gln Gln Asn Gly Arg Pro
 3025 3030 3035 3040

agg cgc gcg ggc gtc tcc gcg ttc gga gtc agc ggg acc aac gcc cac 9168
 Arg Arg Ala Gly Val Ser Ala Phe Gly Val Ser Gly Thr Asn Ala His
 3045 3050 3055

gtc atc atc gag cag gcg ccg gtc gag gcg cac gtc atc agt gag ccg 9216
 Val Ile Ile Glu Gln Ala Pro Val Glu Ala His Val Ile Ser Glu Pro
 3060 3065 3070

gta ccg gct gag gcg cac gtc atc gtc gag cag gcg ccg gtc gag gcg 9264
 Val Pro Ala Glu Ala His Val Ile Val Glu Gln Ala Pro Val Glu Ala
 3075 3080 3085

ccc cac gtg gtc gac gcc acc gga ccg gcg gac ctc acc gag ccg caa 9312
 Pro His Val Val Asp Ala Thr Gly Pro Ala Asp Leu Thr Glu Pro Gln

3090

3095

3100

gag gag gcg gct gaa ccg gag tgc gtc gct gac gcc gtg acc gag atg 9360
 Glu Glu Ala Ala Glu Pro Glu Cys Val Ala Asp Ala Val Thr Glu Met
 3105 3110 3115 3120

tcg gct gaa ccg gag tgc gtc gcc gac gcc atg tcc gag atg tcg gct 9408
 Ser Ala Glu Pro Glu Cys Val Ala Asp Ala Met Ser Glu Met Ser Ala
 3125 3130 3135

gag tgc gtc gcc gag gcc gtg tcc gac aag tcg gct gaa ccg gag tgc 9456
 Glu Cys Val Ala Glu Ala Val Ser Asp Lys Ser Ala Glu Pro Glu Cys
 3140 3145 3150

gtc gcc gac gcc atg tcc gac aag ccg gcc ctc ctg ccc atc ccg tgg 9504
 Val Ala Asp Ala Met Ser Asp Lys Pro Ala Leu Leu Pro Ile Pro Trp
 3155 3160 3165

ctg ctc tcc gcc aag tcc gag cga gcg ctg cgg ggc cag gcg cga cgg 9552
 Leu Leu Ser Ala Lys Ser Glu Arg Ala Leu Arg Gly Gln Ala Arg Arg
 3170 3175 3180

ttg cgg cag ttc gct gcc agg gca tcc gat gcc cgg ccg gcc gac gtg 9600
 Leu Arg Gln Phe Ala Ala Arg Ala Ser Asp Ala Arg Pro Ala Asp Val
 3185 3190 3195 3200

gcg cac gcc ctg gcg gca cag cgg tcc gtg ttc gat cac cgg gcc gtc 9648
 Ala His Ala Leu Ala Ala Gln Arg Ser Val Phe Asp His Arg Ala Val
 3205 3210 3215

gtc gtg gcc gag gac cgc gac ggc ttc ctt cag gcc ctc gac gcg ctg 9696
 Val Val Ala Glu Asp Arg Asp Gly Phe Leu Gln Ala Leu Asp Ala Leu
 3220 3225 3230

gcc gag ggc cgg tcg gcg gac ggc ctg atc gaa ggg tcg gtc ggc ccg 9744
 Ala Glu Gly Arg Ser Ala Asp Gly Leu Ile Glu Gly Ser Val Gly Pro
 3235 3240 3245

cgt ggc ggc cac tca ggc cgc cgg cgc gga aag acc gcc atg ctg ttc 9792
 Arg Gly Gly His Ser Gly Arg Arg Arg Gly Lys Thr Ala Met Leu Phe
 3250 3255 3260

gcc gga cag ggc acg caa cgc gtg gga atg ggc cgt cag ctg tat gcg 9840
 Ala Gly Gln Gly Thr Gln Arg Val Gly Met Gly Arg Gln Leu Tyr Ala
 3265 3270 3275 3280

gct cac ccg gcc tac gcg gac gcg ctg gac cag gta ctg gcg gaa ctg 9888
 Ala His Pro Ala Tyr Ala Asp Ala Leu Asp Gln Val Leu Ala Glu Leu
 3285 3290 3295

gac ggt cac ctg gac cag ccc ctg cgc ccg ctg atc cac gcc agt gcg 9936
 Asp Gly His Leu Asp Gln Pro Leu Arg Pro Leu Ile His Ala Ser Ala
 3300 3305 3310

gat ctt gcg gat gtc gcg gat gcc gcg gat gtt ctg gac cgt acg cgg 9984
 Asp Leu Ala Asp Val Ala Asp Ala Ala Asp Val Leu Asp Arg Thr Arg
 3315 3320 3325

tac gcc cag ccg gcg ctg ttc gcc gtc cag gtc gcg ctc ttc cgg cac 10032
 Tyr Ala Gln Pro Ala Leu Phe Ala Val Gln Val Ala Leu Phe Arg His
 3330 3335 3340

ctg gaa cgt ctc ggc gtg cgc gcg gac ttc gtg gcc ggg cac tcg atc 10080
 Leu Glu Arg Leu Gly Val Arg Ala Asp Phe Val Ala Gly His Ser Ile
 3345 3350 3355 3360

ggc gag ctc gcg gcc gcc cac gtc gcc ggg gtg ctt ccc ctg gca gca 10128
 Gly Glu Leu Ala Ala Ala His Val Ala Gly Val Leu Pro Leu Ala Ala
 3365 3370 3375

gcc tgc cgc ctg gtg gcg gcc cgc ggg cgc ctg atg gag cag ctc gca 10176
 Ala Cys Arg Leu Val Ala Ala Arg Gly Arg Leu Met Glu Gln Leu Ala
 3380 3385 3390

cca ggc ggc gcc atg gtc gcc gta cgg gcg agc gaa gcc gag gcg cga 10224
 Pro Gly Gly Ala Met Val Ala Val Arg Ala Ser Glu Ala Glu Ala Arg

3395	3400	3405	
cag gcg ctc gac ggc cgg gaa gcc cgg gtg tcg gtc gcg gcc gtg aac			10272
Gln Ala Leu Asp Gly Arg Glu Ala Arg Val Ser Val Ala Ala Val Asn			
3410	3415	3420	
gga ccc gcc tcg gtg gtg ttc tcc ggc gcc gag gac gag gtg ggg aac			10320
Gly Pro Ala Ser Val Val Phe Ser Gly Ala Glu Asp Glu Val Gly Asn			
3425	3430	3435	3440
atg gcg gac tgg ttc gcc gag cgc ggg cgg aga gtc aag cgc ctg cga			10368
Met Ala Asp Trp Phe Ala Glu Arg Gly Arg Arg Val Lys Arg Leu Arg			
3445	3450	3455	
acc ggg cat gcc ttc cac tca ccg ctg atg gac ccg atg ctg gag gag			10416
Thr Gly His Ala Phe His Ser Pro Leu Met Asp Pro Met Leu Glu Glu			
3460	3465	3470	
ttc cag cag gtc gcg gcc tcg ctg acc tac agc gaa cca gcc att ccc			10464
Phe Gln Gln Val Ala Ala Ser Leu Thr Tyr Ser Glu Pro Ala Ile Pro			
3475	3480	3485	
atg gtg tcg acg ctc acc ggc gac atc gtg gcg gcg gga gaa ctg agc			10512
Met Val Ser Thr Leu Thr Gly Asp Ile Val Ala Ala Gly Glu Leu Ser			
3490	3495	3500	
gac ccc gag tac tgg gtc cgg cag gta cgg cgg acc gtg cgc ttc ggc			10560
Asp Pro Glu Tyr Trp Val Arg Gln Val Arg Arg Thr Val Arg Phe Gly			
3505	3510	3515	3520
gac gcg atc agc cgc ctg cac acc gac gga gtc cgc acc ttc atg gaa			10608
Asp Ala Ile Ser Arg Leu His Thr Asp Gly Val Arg Thr Phe Met Glu			
3525	3530	3535	
ctg ggc cca gac ggg acc ctg tcg gca ctg gcc gag gaa tgc cta gag			10656
Leu Gly Pro Asp Gly Thr Leu Ser Ala Leu Ala Glu Glu Cys Leu Glu			
3540	3545	3550	

gcc acc gcc gac agc cac ccc gcc gac gac gac acc ggc acc ccg caa 10704
 Ala Thr Ala Asp Ser His Pro Ala Asp Asp Asp Thr Gly Thr Pro Gln
 3555 3560 3565

gag aac ctg ctc atc ccg ctc cta cgg ccg gac agc ccg gaa ccc ggc 10752
 Glu Asn Leu Leu Ile Pro Leu Leu Arg Pro Asp Ser Pro Glu Pro Gly
 3570 3575 3580

acc ctg ctc acc ggc ttg gcc cgg ctg cat acg cac gga gcg gcg gcg 10800
 Thr Leu Leu Thr Gly Leu Ala Arg Leu His Thr His Gly Ala Ala Ala
 3585 3590 3595 3600

gtc aac tgg ccc gcc gcc ctg ccc gaa cgc gat cga gcc cgc cac ctc 10848
 Val Asn Trp Pro Ala Ala Leu Pro Glu Arg Asp Arg Ala Arg His Leu
 3605 3610 3615

gac ctg ccg acc tac gcc ttc gat cac cac cgc tac tgg gtc gac acc 10896
 Asp Leu Pro Thr Tyr Ala Phe Asp His His Arg Tyr Trp Val Asp Thr
 3620 3625 3630

tcg gcc ggc cac ccg ggg gac ctg tcg gca gcg ggg ctc ggc acc gcc 10944
 Ser Ala Gly His Pro Gly Asp Leu Ser Ala Ala Gly Leu Gly Thr Ala
 3635 3640 3645

ggg cat ccc ctg ctc ggt tcc gcg gtg gca ctg gcc gag tcg cag gaa 10992
 Gly His Pro Leu Leu Gly Ser Ala Val Ala Leu Ala Glu Ser Gln Glu
 3650 3655 3660

ctc ctc ttc acc ggc cgt ctc tcc ctg cgc aca cac ccg tgg ctg gcc 11040
 Leu Leu Phe Thr Gly Arg Leu Ser Leu Arg Thr His Pro Trp Leu Ala
 3665 3670 3675 3680

gac cac gcc atc ttc ggt acc gtc ctg ctg ccc ggc acg gcc atc ctg 11088
 Asp His Ala Ile Phe Gly Thr Val Leu Leu Pro Gly Thr Ala Ile Leu
 3685 3690 3695

gaa ctg gcc gtg cgc gca ggc gac gag gtc gac tgc ggc acc gtc gag 11136
 Glu Leu Ala Val Arg Ala Gly Asp Glu Val Asp Cys Gly Thr Val Glu

09914236 002404

3700

3705

3710

gaa ctc acc ctg cgg aca ccg ctc gtc ctt ccc gaa cag ggc tcg gtg 11184
Glu Leu Thr Leu Arg Thr Pro Leu Val Leu Pro Glu Gln Gly Ser Val

3715

3720

3725

atc ctg caa ctc tcc gtc ggg gca ccc cag ggc ccc cag acg ccc gag 11232
Ile Leu Gln Leu Ser Val Gly Ala Pro Gln Gly Pro Gln Thr Pro Glu

3730

3735

3740

gag ccc gaa cgg cgc acc ttc gcc ctg tac gcc cgc gaa gac gac gga 11280
Glu Pro Glu Arg Arg Thr Phe Ala Leu Tyr Ala Arg Glu Asp Asp Gly

3745

3750

3755

3760

ctg tcg tcc tcg tcc gcg gcg gcg acc ggc acc gag tgg acc tgc cac 11328
Leu Ser Ser Ser Ser Ala Ala Ala Thr Gly Thr Glu Trp Thr Cys His

3765

3770

3775

gcc acc ggc gtc ctg acc ggc acc gcc cgg ccc gcg gag gag cac aca 11376
Ala Thr Gly Val Leu Thr Gly Thr Ala Arg Pro Ala Glu Glu His Thr

3780

3785

3790

cag gaa ccg tgg ccg ccc gcc gac gca gca ccg gtg gac ctg gac ggc 11424
Gln Glu Pro Trp Pro Pro Ala Asp Ala Ala Pro Val Asp Leu Asp Gly

3795

3800

3805

tgg tac gag cag ctg gcc ggc gcc ggc ctg gga tac ggg ccg gtg ttc 11472
Trp Tyr Glu Gln Leu Ala Gly Ala Gly Leu Gly Tyr Gly Pro Val Phe

3810

3815

3820

cag ggg ctg cgc gag gtc tgg cgg cgc ggg gac gag gtg ttc gcc gtc 11520
Gln Gly Leu Arg Glu Val Trp Arg Arg Gly Asp Glu Val Phe Ala Val

3825

3830

3835

3840

gtc acc ctg ccc gag agc acg gag gga cag gcg gcc gac gcc gcc cgg 11568
Val Thr Leu Pro Glu Ser Thr Glu Gly Gln Ala Ala Asp Ala Ala Arg

3845

3850

3855

tac gcc ctg cac ccg gcc ctg ctg gac gcg gca ctg cac ccg gtc gtt 11616
Tyr Ala Leu His Pro Ala Leu Leu Asp Ala Ala Leu His Pro Val Val
3860 3865 3870

ctg cgc cac gag ggc gat gcc gcc gcc gac gga cac ggc tgg ctg ccg 11664
Leu Arg His Glu Gly Asp Ala Ala Ala Asp Gly His Gly Trp Leu Pro
3875 3880 3885

ttc tcc tgg acc ggc gtc acg gtc gcc gcc tcc ggc gcc tcc acc ctg 11712
Phe Ser Trp Thr Gly Val Thr Val Ala Ala Ser Gly Ala Ser Thr Leu
3890 3895 3900

cac gtc cgt ctc acc gtc cgc acg gac gag gac gcg gtc gga ctg ctg 11760
His Val Arg Leu Thr Val Arg Thr Asp Glu Asp Ala Val Gly Leu Leu
3905 3910 3915 3920

gcc acc gac gca tcg gga cgc atc gtc atc tcc gcg ggg tcc ctc gcc 11808
Ala Thr Asp Ala Ser Gly Arg Ile Val Ile Ser Ala Gly Ser Leu Ala
3925 3930 3935

ttc cgg ccc gtc tcc gcc gag cag ctc cag gcc gcg cgc acc ggc tac 11856
Phe Arg Pro Val Ser Ala Glu Gln Leu Gln Ala Ala Arg Thr Gly Tyr
3940 3945 3950

cac gac cac ctc ttc cgc atc gaa tgg cgg ccg ctg cac ctc ccc acc 11904
His Asp His Leu Phe Arg Ile Glu Trp Arg Pro Leu His Leu Pro Thr
3955 3960 3965

aca ccg gca cgg aca gcc gac tgg gcc cta atc ggc ccc ggt gcc cgg 11952
Thr Pro Ala Arg Thr Ala Asp Trp Ala Leu Ile Gly Pro Gly Ala Arg
3970 3975 3980

cgg acg gcc gcc gtc ctg gag cgc aac ggc gcc tcc tgg cag gcc tac 12000
Arg Thr Ala Ala Val Leu Glu Arg Asn Gly Ala Ser Trp Gln Ala Tyr
3985 3990 3995 4000

ccg gac ccg gcg gct ctc gca gaa gcc ctg gcg gcc ggc gcc ccg gca 12048
Pro Asp Pro Ala Ala Leu Ala Glu Ala Leu Ala Ala Gly Ala Pro Ala

4005

4010

4015

ccg ggc atg gtc gtc atc tcg tgc gag ccg gac ggc gca tcc gcc ccc 12096
Pro Gly Met Val Val Ile Ser Cys Glu Pro Asp Gly Ala Ser Ala Pro

4020

4025

4030

acc gat tcc gcc ctc acc gat tcc gcc ctc acc gat tcc gcc ccg gcc 12144
Thr Asp Ser Ala Leu Thr Asp Ser Ala Leu Thr Asp Ser Ala Pro Ala

4035

4040

4045

ggc tcg gcc ccg gcc gac tcc acc gcc ctc gcc gac gcc acc cgg caa 12192
Gly Ser Ala Pro Ala Asp Ser Thr Ala Leu Ala Asp Ala Thr Arg Gln

4050

4055

4060

gcc acc acc cgc gtc ctc gcc ctg ctc cag gaa tgg gtc gcc gac gaa 12240
Ala Thr Thr Arg Val Leu Ala Leu Leu Gln Glu Trp Val Ala Asp Glu

4065

4070

4075

4080

cgg ctc gcg gcc tgc cgc ctg gcc ctc ctc acg cac ggc tcg gtc acc 12288
Arg Leu Ala Ala Cys Arg Leu Ala Leu Leu Thr His Gly Ser Val Thr

4085

4090

4095

gcg acc ccc gac gag ccc gtg tcc gac ctc gca cac gcc gcc gtc tgg 12336
Ala Thr Pro Asp Glu Pro Val Ser Asp Leu Ala His Ala Ala Val Trp

4100

4105

4110

gga ctg gtc cgc tcc gtg cag acc gag aac ccc gac cgg ttc ctg ctg 12384
Gly Leu Val Arg Ser Val Gln Thr Glu Asn Pro Asp Arg Phe Leu Leu

4115

4120

4125

gcc gac acc gac gac acc gac gcc tcc cgc aac gcc ctt ccc ctg ctg 12432
Ala Asp Thr Asp Asp Thr Asp Ala Ser Arg Asn Ala Leu Pro Leu Leu

4130

4135

4140

gcc ggg gaa ccg cag atc gcc ctg cga aat ggt gcc gtc cgc atc ccg 12480
Ala Gly Glu Pro Gln Ile Ala Leu Arg Asn Gly Ala Val Arg Ile Pro

4145

4150

4155

4160

cgg atg aca cga gtg ccc gtc cgg cag cca cag ccg agc acc acc gac 12528
 Arg Met Thr Arg Val Pro Val Arg Gln Pro Gln Pro Ser Thr Thr Asp
 4165 4170 4175

gcc gac tgg gac ccg gag gcc acg gtc ctc atc acg ggc ggt acc ggc 12576
 Ala Asp Trp Asp Pro Glu Ala Thr Val Leu Ile Thr Gly Gly Thr Gly
 4180 4185 4190

gtc ctc ggc cgg ctc gtc gcc cgt cat ctc gcc acg gcc cac ggg gta 12624
 Val Leu Gly Arg Leu Val Ala Arg His Leu Ala Thr Ala His Gly Val
 4195 4200 4205

cgg cac ctg ctg ctg gcc acc cgc cgc ggc acg gcc gcg gac ggc gcc 12672
 Arg His Leu Leu Leu Ala Thr Arg Arg Gly Thr Ala Ala Asp Gly Ala
 4210 4215 4220

gcc gac ctg gtc gcc gaa ctc gcc ggc ctc ggc gcc gag gcc acg gtc 12720
 Ala Asp Leu Val Ala Glu Leu Ala Gly Leu Gly Ala Glu Ala Thr Val
 4225 4230 4235 4240

gcg gcc tgc gac atc ggg gac cgg gcg gcc gtc gcc gcg ctc ctc gac 12768
 Ala Ala Cys Asp Ile Gly Asp Arg Ala Ala Val Ala Ala Leu Leu Asp
 4245 4250 4255

caa gtg ccc gcg cag cac ccc ctg aaa gcc gtg atc cac acg gcc ggt 12816
 Gln Val Pro Ala Gln His Pro Leu Lys Ala Val Ile His Thr Ala Gly
 4260 4265 4270

gtg gtc gac gac ggc atc ctc acc tcg ctc act ccg gag cgc atg gag 12864
 Val Val Asp Asp Gly Ile Leu Thr Ser Leu Thr Pro Glu Arg Met Glu
 4275 4280 4285

gcc gtc ctg cac gcg aag gcg ttc ggc gcc gcg cac ctg cac gac ctg 12912
 Ala Val Leu His Ala Lys Ala Phe Gly Ala Ala His Leu His Asp Leu
 4290 4295 4300

acc cgc gac gcc ggc ctc acc acc ttc acc gtc ttc tcc tcg gcc gcc 12960
 Thr Arg Asp Ala Gly Leu Thr Thr Phe Thr Val Phe Ser Ser Ala Ala

104280" 98241650

4305	4310	4315	4320
gcc tcc ttc ggc agt ccc gga cag ggc aac tac acc gcg gcg aac gcc 13008			
Ala Ser Phe Gly Ser Pro Gly Gln Gly Asn Tyr Thr Ala Ala Asn Ala			
4325	4330	4335	
ttt ctg gac gcc ctg atg cag cac cgc cac acc cag gca ctg ccg ggc 13056			
Phe Leu Asp Ala Leu Met Gln His Arg His Thr Gln Ala Leu Pro Gly			
4340	4345	4350	
cgg tcg ctc gcc tgg ggc ctt tgg ggc gag gcc gac ggc atg acc cgc 13104			
Arg Ser Leu Ala Trp Gly Leu Trp Gly Glu Ala Asp Gly Met Thr Arg			
4355	4360	4365	
aac ctc gcc ggc acc gac ttc gcg cgc atg gcc cgc ggc ggc ctg ctc 13152			
Asn Leu Ala Gly Thr Asp Phe Ala Arg Met Ala Arg Gly Gly Leu Leu			
4370	4375	4380	
ccc ctg tcc aac gca cag gga ctc gcg ctc ctc gac aca gcg gat cgc 13200			
Pro Leu Ser Asn Ala Gln Gly Leu Ala Leu Leu Asp Thr Ala Asp Arg			
4385	4390	4395	4400
ctc ggc cct ttc ggt gac ggg ctg ctc ctc gcc acc cgg ctc gac gcg 13248			
Leu Gly Pro Phe Gly Asp Gly Leu Leu Leu Ala Thr Arg Leu Asp Ala			
4405	4410	4415	
gcc acc ctc cac gca cag gcc acg gcc ggc gcc ctg ccg cgc atc ctg 13296			
Ala Thr Leu His Ala Gln Ala Thr Ala Gly Ala Leu Pro Arg Ile Leu			
4420	4425	4430	
cac ggg ctg atc cgc atc ccg gcc cgg cgg tcc gcc gac cac ggc atc 13344			
His Gly Leu Ile Arg Ile Pro Ala Arg Arg Ser Ala Asp His Gly Ile			
4435	4440	4445	
gcg acc gac acc ccc gcc acg ctg cgc gag cgc ctg gcc gga ctc acc 13392			
Ala Thr Asp Thr Pro Ala Thr Leu Arg Glu Arg Leu Ala Gly Leu Thr			
4450	4455	4460	

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4610	4615	4620	
ctg ctc tcg gcg gcc tcc ttc ttc cgg ccc gcc ttc acg gac ccc tcg			13920
Leu Leu Ser Ala Ala Ser Phe Phe Arg Pro Ala Phe Thr Asp Pro Ser			
4625	4630	4635	4640
gac atc ccg gag ccg acg ttc gtc cgg ctc gcc cag ggt gaa gcg cgc			13968
Asp Ile Pro Glu Pro Thr Phe Val Arg Leu Ala Gln Gly Glu Ala Arg			
4645	4650	4655	
gcc caa ggt gaa gca ctc gcc cgg ggc gaa aca cgg ccc gcc ctc atc			14016
Ala Gln Gly Glu Ala Leu Ala Arg Gly Glu Thr Arg Pro Ala Leu Ile			
4660	4665	4670	
tgc ctg ccc acc gtc gcc gcc gtg tcg agc gtg tac cag tac tca cgt			14064
Cys Leu Pro Thr Val Ala Ala Val Ser Ser Val Tyr Gln Tyr Ser Arg			
4675	4680	4685	
ttc gcg gcg gga ctg aac gga cac cga gac gtc tgg tac gtt cct gcg			14112
Phe Ala Ala Gly Leu Asn Gly His Arg Asp Val Trp Tyr Val Pro Ala			
4690	4695	4700	
cca ggg ttc ctg gag ggc gaa ccc ctg ccg tcc gga atc ggc gcg gtg			14160
Pro Gly Phe Leu Glu Gly Glu Pro Leu Pro Ser Gly Ile Gly Ala Val			
4705	4710	4715	4720
acc cgc atg ttc gcc gac gcg atc gtc cgg ttc acc gac ggc gcg cct			14208
Thr Arg Met Phe Ala Asp Ala Ile Val Arg Phe Thr Asp Gly Ala Pro			
4725	4730	4735	
ttt gcg ctc gcc ggg cat tcc gcg ggc gga tgg ttc gtc tac gcg gtg			14256
Phe Ala Leu Ala Gly His Ser Ala Gly Gly Trp Phe Val Tyr Ala Val			
4740	4745	4750	
acg agt cat ctg gag cgt cta ggc gtc cgt ccg gaa gcg gtg gtg acc			14304
Thr Ser His Leu Glu Arg Leu Gly Val Arg Pro Glu Ala Val Val Thr			
4755	4760	4765	

atg gac gcc tat ctc ccg gac gac ggc atc gca cct gtc gcg tcc gcg 14352
Met Asp Ala Tyr Leu Pro Asp Asp Gly Ile Ala Pro Val Ala Ser Ala
4770 4775 4780

ctg aca agt gaa atc ttc gac cgc gtc acg cag ttt gtg gac gtg gac 14400
Leu Thr Ser Glu Ile Phe Asp Arg Val Thr Gln Phe Val Asp Val Asp
4785 4790 4795 4800

tac aca cgc ctg gtc gcc atg ggc gga tac ttc cgc atc ttc tcc ggc 14448
Tyr Thr Arg Leu Val Ala Met Gly Gly Tyr Phe Arg Ile Phe Ser Gly
4805 4810 4815

tgg agt cct ccg gac atc acc aca ccc gcc ctc ttc ctg cgc ggc cgg 14496
Trp Ser Pro Pro Asp Ile Thr Thr Pro Ala Leu Phe Leu Arg Gly Arg
4820 4825 4830

gac gga gaa cag atg ccg ccg ccg tgg gga gtt ccg cac acc gtt ctg 14544
Asp Gly Glu Gln Met Pro Pro Pro Trp Gly Val Pro His Thr Val Leu
4835 4840 4845

gac atc cag ggg aat cac ttc acg atg ctg gaa cag ttt gcg gat tcg 14592
Asp Ile Gln Gly Asn His Phe Thr Met Leu Glu Gln Phe Ala Asp Ser
4850 4855 4860

act gct cgg cat gtc gac gaa tgg ctg aca gaa atc gca tca gtg cgg 14640
Thr Ala Arg His Val Asp Glu Trp Leu Thr Glu Ile Ala Ser Val Arg
4865 4870 4875 4880

cgc tgatcgcgcc tctgatcgcg gtccgatcg cgccctgat cggcgggtcg 14693
Arg

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catcgatcag tgctttcccc ctacggcca tacgggcctt tctgagactt cttgaatttg 14813

ggagacagtg atg gac acg tcc agc gaa aag ctc gtc gac gcg ctt agg 14862
Met Asp Thr Ser Ser Glu Lys Leu Val Asp Ala Leu Arg
4885 4890

gcg tct ctg aag gcg aac cag acc ctg cgg gca cgt aat gag caa ctg	14910
Ala Ser Leu Lys Ala Asn Gln Thr Leu Arg Ala Arg Asn Glu Gln Leu	
4895 4900 4905 4910	
gca gcc gcc atg gag gcg tcc agc gag ccg att gcg att gtg ggg atg	14958
Ala Ala Ala Met Glu Ala Ser Ser Glu Pro Ile Ala Ile Val Gly Met	
4915 4920 4925	
gcg tgt cgt ttt ccg ggt ggg gtg tgt tcg ccg gag gag ttg tgg gag	15006
Ala Cys Arg Phe Pro Gly Gly Val Cys Ser Pro Glu Glu Leu Trp Glu	
4930 4935 4940	
ctg gtt gcg tcg ggt ggg gat gcg att ggt gaa ttt ccg gcc ggt cgg	15054
Leu Val Ala Ser Gly Gly Asp Ala Ile Gly Glu Phe Pro Ala Gly Arg	
4945 4950 4955	
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Gly Trp Asp Leu Glu Gly Leu Phe Asp Ser Asp Pro Asp Arg Ser Gly	
4960 4965 4970	
acg tcg tac gcg cgg tat ggc ggg ttt ttg tat gag gcg ggg gag ttc	15150
Thr Ser Tyr Ala Arg Tyr Gly Gly Phe Leu Tyr Glu Ala Gly Glu Phe	
4975 4980 4985 4990	
gat gcg gac ttc ttc ggg atc agt ccg cgt gag gcg ttg gcg atg gat	15198
Asp Ala Asp Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp	
4995 5000 5005	
ccg cag cag cgg ttg ttg ctg gag acg tcg tgg gag gcg ttc gag cgg	15246
Pro Gln Gln Arg Leu Leu Leu Glu Thr Ser Trp Glu Ala Phe Glu Arg	
5010 5015 5020	
gcg ggt atc gat ccg ctg tcg atg cgt ggc tcc cgt acg ggt gtc ttc	15294
Ala Gly Ile Asp Pro Leu Ser Met Arg Gly Ser Arg Thr Gly Val Phe	
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gcc ggg gtg atg tac cac gac tac gga tcc cgc ctg ggt acc atc ccc	15342
Ala Gly Val Met Tyr His Asp Tyr Gly Ser Arg Leu Gly Thr Ile Pro	

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gag gga ttc gag ggc tac atc ggc aac ggt agc ggc ggc gcc gtc gcg 15390
 Glu Gly Phe Glu Gly Tyr Ile Gly Asn Gly Ser Gly Gly Ala Val Ala

5055

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5070

tcg ggc cgc gtc gcc tac acg ctc ggt ctc gag ggc cct gcc gtc tcg 15438
 Ser Gly Arg Val Ala Tyr Thr Leu Gly Leu Glu Gly Pro Ala Val Ser

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5085

gtg gac acg gca tgt tcg tcg tcg ttg gtg gcg ctg cat ctg gcg tgc 15486
 Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys

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5095

5100

cag tcg ctg cgg tcg ggt gag tgc acg ctc gcg ctg gcc ggc ggt gtg 15534
 Gln Ser Leu Arg Ser Gly Glu Cys Thr Leu Ala Leu Ala Gly Gly Val

5105

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5115

acg gtg atg tcg acc ccg cac ctc ttc gtc gag ttc tca cgc cag cgc 15582
 Thr Val Met Ser Thr Pro His Leu Phe Val Glu Phe Ser Arg Gln Arg

5120

5125

5130

gga ctg tcg gtg gac ggc cgc tgc aag tcc ttc gcg ggt gga gcc gac 15630
 Gly Leu Ser Val Asp Gly Arg Cys Lys Ser Phe Ala Gly Gly Ala Asp

5135

5140

5145

5150

ggc acc ggc atg ggc gag ggc gtc ggg atg ctg ttg gtg gag cgg ttg 15678
 Gly Thr Gly Met Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu

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5165

tcg gat gcg gtg cgg ctg ggg cat cgg gtg ctg gcg gtg ctg cgc ggc 15726
 Ser Asp Ala Val Arg Leu Gly His Arg Val Leu Ala Val Leu Arg Gly

5170

5175

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agt gcg gtc aat cag gac ggt gcg tcg aat ggg ttg acg gcg ccg aat 15774
 Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn

5185

5190

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ggt ccg gct cag gag cgg gtg atc cgg cag gcg ttg gcg aac gcg ggg 15822
 Gly Pro Ala Gln Glu Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly
 5200 5205 5210

ttg tcc gtg gcg gat gtg gat gtg gtg gag ggg cat ggg acg ggc acg 15870
 Leu Ser Val Ala Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr
 5215 5220 5225 5230

acg ctg ggt gat ccg atc gag gcg cag gcg ttg ctc gcc acg tac ggg 15918
 Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly
 5235 5240 5245

cag cgg gcc ggt aac agg ccg ctg tgg ctg gga tcg gtg aag tcg aac 15966
 Gln Arg Ala Gly Asn Arg Pro Leu Trp Leu Gly Ser Val Lys Ser Asn
 5250 5255 5260

atc ggc cat gcg cag gct gcc gcg ggt gtg ggt ggg gtc atc aag atg 16014
 Ile Gly His Ala Gln Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met
 5265 5270 5275

gtg atg gcg ttg ccg gag ggg gtg ttg ccg cgg acg ttg cat gtg gat 16062
 Val Met Ala Leu Arg Glu Gly Val Leu Pro Arg Thr Leu His Val Asp
 5280 5285 5290

gag ccg tcg ccg cag gtg gac tgg tcc gcg ggg gcg gtg cgg ctg ctg 16110
 Glu Pro Ser Pro Gln Val Asp Trp Ser Ala Gly Ala Val Arg Leu Leu
 5295 5300 5305 5310

acg gag gcg gtg ccg tgg ccg ggg gac gcg gca ggg cgg ttg cgg cgg 16158
 Thr Glu Ala Val Pro Trp Pro Gly Asp Ala Ala Gly Arg Leu Arg Arg
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gcg gga gtg tcg tcg ttc ggg gtc agt ggc acg aat gcg cat gtg att 16206
 Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile
 5330 5335 5340

ttg gag gag gcg ccg gcg gcg ggg ggc tgt gtt gcc ggg ggt ggg gtg 16254
 Leu Glu Glu Ala Pro Ala Ala Gly Gly Cys Val Ala Gly Gly Gly Val

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Leu Glu Gly Ala Pro Gly Leu Ala Ile Ser Val Ala Glu Ser Val Ala			
5360	5365	5370	
gct cca gtg gct gtg tct gcg ccg gtg gct gag tcg gtg ccg gtg ccg			16350
Ala Pro Val Ala Val Ser Ala Pro Val Ala Glu Ser Val Pro Val Pro			
5375	5380	5385	5390
gtg ccg gtg ccg gtt cct gtg ccg gtg tcg gct agg tct gag gct ggg			16398
Val Pro Val Pro Val Pro Val Pro Val Ser Ala Arg Ser Glu Ala Gly			
5395	5400	5405	
ttg cgg gcg cag gcg gag gcg ttg cgt cag tac gtg gca gtc cgg ccg			16446
Leu Arg Ala Gln Ala Glu Ala Leu Arg Gln Tyr Val Ala Val Arg Pro			
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gac gtt tcg ctt gcc gat gtg ggt gcg ggt ctg gcc tgt ggg ccg gct			16494
Asp Val Ser Leu Ala Asp Val Gly Ala Gly Leu Ala Cys Gly Arg Ala			
5425	5430	5435	
gtg ctg gag cat cgt gcg gtc gtc ctg gcc gcg gac cgt gag gag ctg			16542
Val Leu Glu His Arg Ala Val Val Leu Ala Ala Asp Arg Glu Glu Leu			
5440	5445	5450	
gtg caa ggg ttg ggg gcg ctg gcg gcg ggt gag ccg gat ccg ccg gtg			16590
Val Gln Gly Leu Gly Ala Leu Ala Ala Gly Glu Pro Asp Arg Arg Val			
5455	5460	5465	5470
acc acg ggt cat gcg ccg ggt ggt gac ccg ggc ggt gtc gtc ttc gtg			16638
Thr Thr Gly His Ala Pro Gly Gly Asp Arg Gly Gly Val Val Phe Val			
5475	5480	5485	
ttt ccc gga cag ggt ggg cag tgg gcc ggg atg ggt gtg cgt ctg ctc			16686
Phe Pro Gly Gln Gly Gly Gln Trp Ala Gly Met Gly Val Arg Leu Leu			
5490	5495	5500	

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 Leu Ala Pro Trp Val Asp Trp Ser Val Val Asp Ile Leu Arg Arg Asp
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 Ala Gly Asp Ala Val Trp Glu Arg Ala Asp Val Val Gln Pro Val Leu
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 Phe Ser Val Met Val Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Ile
 5555 5560 5565

gaa ccc gac gcg gtc ctt ggc cat tcc cag ggc gag atc gcg gcc gcg 16926
 Glu Pro Asp Ala Val Leu Gly His Ser Gln Gly Glu Ile Ala Ala Ala
 5570 5575 5580

cat gtg tgt ggg gcg ctg agc ctg aag gac gcg gcg aag act gtt gcg 16974
 His Val Cys Gly Ala Leu Ser Leu Lys Asp Ala Ala Lys Thr Val Ala
 5585 5590 5595

ctg cgc agc cgg gcg ctg gcc gct gtg cgg ggc cgg ggc ggc atg gcc 17022
 Leu Arg Ser Arg Ala Leu Ala Ala Val Arg Gly Arg Gly Gly Met Ala
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tca gtg ccg ctg cct gcc cag gag gtg gag cag ctc att ggt gag cgg 17070
 Ser Val Pro Leu Pro Ala Gln Glu Val Glu Gln Leu Ile Gly Glu Arg
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 Trp Ala Gly Arg Leu Trp Val Ala Ala Val Asn Gly Pro Arg Ser Thr
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 Ala Val Ser Gly Asp Ala Glu Ala Val Asp Glu Val Leu Ala Tyr Cys

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5655

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gcc ggc acc ggg gtg cgg gcc cgg cgg atc ccg gtc gac tat gcc tgc 17214
Ala Gly Thr Gly Val Arg Ala Arg Arg Ile Pro Val Asp Tyr Ala Ser

5665

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5675

cac tgc ccc cat gtg cag ccc ctg cgg gag gag ttg ctg gag ctg ctg 17262
His Cys Pro His Val Gln Pro Leu Arg Glu Glu Leu Leu Glu Leu Leu

5680

5685

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Gly Asp Ile Ser Pro Gln Pro Ser Gly Val Pro Phe Phe Ser Thr Val

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5705

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gag ggc acc tgg ctg gac acc aca acc ctg gac gcc gcc tac tgg tac 17358
Glu Gly Thr Trp Leu Asp Thr Thr Thr Leu Asp Ala Ala Tyr Trp Tyr

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5725

cgc aac ctg cac cag cct gtc cgt ttc agc gat gcc gtc cag gcc ctg 17406
Arg Asn Leu His Gln Pro Val Arg Phe Ser Asp Ala Val Gln Ala Leu

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5735

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gcg gat gac gga cac cgc gtc ttc gtc gaa gtc agc ccc cac ccc acc 17454
Ala Asp Asp Gly His Arg Val Phe Val Glu Val Ser Pro His Pro Thr

5745

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ctc gtc ccc gcc atc gaa gac acc acc gaa gac acc gcc gaa gac gtc 17502
Leu Val Pro Ala Ile Glu Asp Thr Thr Glu Asp Thr Ala Glu Asp Val

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5765

5770

acc gcg atc ggc agc ctc cgc cgc ggc gac aac gac acc cgc cgc ttc 17550
Thr Ala Ile Gly Ser Leu Arg Arg Gly Asp Asn Asp Thr Arg Arg Phe

5775

5780

5785

5790

ctc acc gcc ctc gcc cac acc cac acc acc ggc atc ggc aca ccc acc 17598
Leu Thr Ala Leu Ala His Thr His Thr Thr Gly Ile Gly Thr Pro Thr

5795

5800

5805

acc tgg cac cac cac tac acc cac cac cac acc cac ccc cac aac cac 17646
 Thr Trp His His His Tyr Thr His His His Thr His Pro His Asn His
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 His Leu Asp Leu Pro Thr Tyr Pro Phe Gln Arg Gln His Tyr Trp Leu
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gac gct ccc acg gga gca ggt gac gtc gcc gct gct ggc ttg gag ccg 17742
 Asp Ala Pro Thr Gly Ala Gly Asp Val Ala Ala Ala Gly Leu Glu Pro
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gcc gaa cac cct ctg ctc gcg gca aca gtc caa ctc gca gac acg gac 17790
 Ala Glu His Pro Leu Leu Ala Ala Thr Val Gln Leu Ala Asp Thr Asp
 5855 5860 5865 5870

ggc tgc cta ctg acg ggt cgc ctg tcc ttg cgc tcg cat ccg tgg ctg 17838
 Gly Cys Leu Leu Thr Gly Arg Leu Ser Leu Arg Ser His Pro Trp Leu
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 Gly Asp Tyr Glu Val Gly Gly Ala Val Leu Leu Ser Gly Ser Ala Phe
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 Val Glu Leu Ala Val Gln Val Gly Glu Arg Val Gly Cys Thr Arg Ile
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 Glu Gln Leu Thr Val His Ala Pro Leu Val Val Pro Val Gly Gly Gly
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ggg ttt ggg gag ggg gcg ggg ttc ggg gag ggt gtt cgg gtg ccg gct 18462
 Gly Phe Gly Glu Gly Ala Gly Phe Gly Glu Gly Val Arg Val Pro Ala
 6080 6085 6090

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 Val Trp Gly Gly Val Ser Leu His Arg Ala Gly Val Thr Gly Val Arg
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Val Arg Val Trp Ala Val Gly Arg Gly Gly Gly Arg Glu Ala Val Ser
6115 6120 6125

gtc gtg gtc ggg gat gag gcg ggt gtg ccg gtg gcg tcg gtc gat cgt 18606
Val Val Val Gly Asp Glu Ala Gly Val Pro Val Ala Ser Val Asp Arg
6130 6135 6140

ctt gag ttg cgg cct gtg gat atg ggt cag ttg cgt gct gtc tcg gtt 18654
Leu Glu Leu Arg Pro Val Asp Met Gly Gln Leu Arg Ala Val Ser Val
6145 6150 6155

tcg gcg ggg cgg cgg ggt tcg ctg tat gcg gtg cag tgg gct gag gtg 18702
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6160 6165 6170

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6175 6180 6185 6190

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6195 6200 6205

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Pro Asp Ala Gly Ala Gly Gly Gly Gly Gly Gly Val Gly Glu Val
6210 6215 6220

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6225 6230 6235

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Phe Ala Gly Ser Arg Leu Val Val Val Thr Arg Gly Ala Val Val Ala
6240 6245 6250

ggc caa gaa gac ggc ccg gtg gat gtg gtg ggt gcg gcg gtg tgg ggg 18990
Gly Gln Glu Asp Gly Pro Val Asp Val Val Gly Ala Ala Val Trp Gly

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ctg gtg cgg tcg gcg cag gct gag cat ccg gac cgg ttt gtc ctc ctc 19038

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6280

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Asp Leu Asp Thr Asp Thr Asp Thr Gly Thr Asp Leu Asp Thr Gly Ala

6290

6295

6300

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6305

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Ala Val Val Ala Cys Gly Glu Pro Gln Leu Ala Val Arg Gly Glu Arg

6320

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Val Leu Ala Ala Arg Leu Thr Arg Leu Glu Ser Ser Val Asp Val Pro

6335

6340

6345

6350

gct cag cgg tcc ggt gat gtt gct ggt cgg gag gtg ttg ccg tgg ttg 19278

Ala Gln Arg Ser Gly Asp Val Ala Gly Arg Glu Val Leu Pro Trp Leu

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Ala Val Ala Arg His Leu Ala Gly Val Cys Gly Val Arg Asp Leu Leu

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6410

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gtg ggg gag cgg cgg gag gtg gtc cgg ctg ctg gag ggt gtt cct gcc 19518
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 Gly Cys Pro Leu Thr Gly Val Val His Ala Ala Gly Val Leu Asp Asp
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 Ala Thr Ile Ala Ser Leu Thr Pro Glu Arg Leu Gly Thr Val Phe Ala
 6465 6470 6475

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 6480 6485 6490

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 Glu Leu Ser Ala Phe Val Leu Phe Ser Ser Ala Ala Gly Ile Leu Gly
 6495 6500 6505 6510

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 Ser Ala Gly Gln Gly Asn Tyr Ala Ala Ala Asn Ala Ala Leu Asp Ala
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 Trp Gly Leu Trp Glu Glu Ala Ser Gly Met Thr Gly His Leu Ala Gly
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 Thr Asp His Arg Arg Ile Ile Arg Ser Gly Leu His Pro Met Ser Thr

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ccg gac gca ctg gct ctc ttc gat gcg gcc ctg gct ctg gac cgg ccg 19950

Pro Asp Ala Leu Ala Leu Phe Asp Ala Ala Leu Ala Leu Asp Arg Pro

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Val Leu Leu Pro Ala Asp Leu Arg Pro Ala Pro Pro Leu Pro Pro Leu

6595

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Leu Gln Asp Leu Leu Pro Ala Thr Arg Arg Arg Thr Thr Arg Thr Thr

6610

6615

6620

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Thr Thr Gly Gly Ala Asp Asn Gly Ala Gln Leu His Ala Arg Leu Ala

6625

6630

6635

ggc cag aca cac gaa caa cag cac acc acc ctc ctc gcc ctg gtc cgc 20142

Gly Gln Thr His Glu Gln Gln His Thr Thr Leu Leu Ala Leu Val Arg

6640

6645

6650

tcc cac atc gcc acc gtc ctc ggc cac acc acc ccc gac acc atc ccc 20190

Ser His Ile Ala Thr Val Leu Gly His Thr Thr Pro Asp Thr Ile Pro

6655

6660

6665

6670

ccc gac cgc gcg ttc cgc gac ctc ggc ttc gac tcc ctc acc gcc gtc 20238

Pro Asp Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val

6675

6680

6685

gaa cta cgc aac cgg ctc tcc cgc acc acc gga ctc cgc ctc ccc acc 20286

Glu Leu Arg Asn Arg Leu Ser Arg Thr Thr Gly Leu Arg Leu Pro Thr

6690

6695

6700

acc ctc gcc ttc gac cac ccc aac ccc acc acc ctc acc cac cac ctc 20334

Thr Leu Ala Phe Asp His Pro Asn Pro Thr Thr Leu Thr His His Leu

6705

6710

6715

cac aca caa ctt ctg ggc tcg gac agc act gcc tcc atc cca gct ccc 20382
 His Thr Gln Leu Leu Gly Ser Asp Ser Thr Ala Ser Ile Pro Ala Pro
 6720 6725 6730

cgt gct gcg gct gtg cct gca gac cag gac gag ccc gtc gcg atc att 20430
 Arg Ala Ala Ala Val Pro Ala Asp Gln Asp Glu Pro Val Ala Ile Ile
 6735 6740 6745 6750

ggc atg gcg tgc cgc tat ccc gga ggc gtc acc tca gcc gag gag ctg 20478
 Gly Met Ala Cys Arg Tyr Pro Gly Gly Val Thr Ser Ala Glu Glu Leu
 6755 6760 6765

tgg gaa ctg ctc gca tcg ggg agg gac acg gtc ggc gag ttt ccg acg 20526
 Trp Glu Leu Leu Ala Ser Gly Arg Asp Thr Val Gly Glu Phe Pro Thr
 6770 6775 6780

gac cgt ggg tgg gac ctg gaa gca ctg ttc gat ccg gaa ccg ggt ccg 20574
 Asp Arg Gly Trp Asp Leu Glu Ala Leu Phe Asp Pro Glu Pro Gly Arg
 6785 6790 6795

ccg ggc acc tcg tac acc cgt tgt ggg agt ttc ctc tac gac gcg ggg 20622
 Pro Gly Thr Ser Tyr Thr Arg Cys Gly Ser Phe Leu Tyr Asp Ala Gly
 6800 6805 6810

gag ttc gac gcc ggc ttc ttc ggg atc agt ccg cgt gag gca ctg gcg 20670
 Glu Phe Asp Ala Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala
 6815 6820 6825 6830

atg gac ccg cag cag cga ttg ctg ctg gag gcc tca tgg gag gcc atg 20718
 Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Ala Ser Trp Glu Ala Met
 6835 6840 6845

gag cag gca ggt att gac cct acg acc gta cgc ggg agc cag aca ggc 20766
 Glu Gln Ala Gly Ile Asp Pro Thr Thr Val Arg Gly Ser Gln Thr Gly
 6850 6855 6860

gtg ttc gcg ggc ctc att ccg cag gcc tat gga ccc agg ctg cac gaa 20814
 Val Phe Ala Gly Leu Ile Pro Gln Ala Tyr Gly Pro Arg Leu His Glu

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09914286 08241660

6865	6870	6875	
aac gcc gca gcc gac acc gag ggc tat gtc ctg acc ggc aca tcc ggg			20862
Asn Ala Ala Ala Asp Thr Glu Gly Tyr Val Leu Thr Gly Thr Ser Gly			
6880	6885	6890	
agt gtg gcc tcc ggt cgt atc tcg tac acg ttt ggt ttt gag ggt cct			20910
Ser Val Ala Ser Gly Arg Ile Ser Tyr Thr Phe Gly Phe Glu Gly Pro			
6895	6900	6905	6910
gcg gtg tcg gtg gac acg gct tgt tcc tcg tcg ttg gtg gct tta cat			20958
Ala Val Ser Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His			
6915	6920	6925	
ctg gcc tgt cag gcg ttg cgt gcg ggt gag tgc tcg atg gcg ctt gcc			21006
Leu Ala Cys Gln Ala Leu Arg Ala Gly Glu Cys Ser Met Ala Leu Ala			
6930	6935	6940	
ggg ggt gtg acg gtg atg tcg tct ccg ggt gcc ttc gtg gag ttt tcg			21054
Gly Gly Val Thr Val Met Ser Ser Pro Gly Ala Phe Val Glu Phe Ser			
6945	6950	6955	
cgg cag cgg ggt ctg gcc gcg gac ggg cat tgc aag gcg ttc tcg gcg			21102
Arg Gln Arg Gly Leu Ala Ala Asp Gly His Cys Lys Ala Phe Ser Ala			
6960	6965	6970	
gcg gcg gac ggg acc ggc tgg ggt gag ggt gtg ggg atg ctg ctg gtg			21150
Ala Ala Asp Gly Thr Gly Trp Gly Glu Gly Val Gly Met Leu Leu Val			
6975	6980	6985	6990
gag cgg ctc tcc gac gcc cgt cgc aac ggt cac cgt gtc ctg gcc gtg			21198
Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly His Arg Val Leu Ala Val			
6995	7000	7005	
gtg cgt ggc agt gcg gtc aac cag gac ggt gcg agc aac ggg ctg acc			21246
Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr			
7010	7015	7020	

gcg ccc aac ggg ccc tcc cag cag cgt gtc atc cgc cag gcc ctc gcc 21294
 Ala Pro Asn Gly Pro Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala
 7025 7030 7035

aac gcc ggc ttg tcg gcc ggt gat gtc gat gcg gtg gag gcc cac ggc 21342
 Asn Ala Gly Leu Ser Ala Gly Asp Val Asp Ala Val Glu Ala His Gly
 7040 7045 7050

acc ggc acc act ttg ggc gac ccg atc gag gcc cag gcc ctc ctt gcg 21390
 Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala
 7055 7060 7065 7070

acc tac ggg cag gac cgt gcc ggc gag ggg ccg ctg tgg ctg ggc tcg 21438
 Thr Tyr Gly Gln Asp Arg Ala Gly Glu Gly Pro Leu Trp Leu Gly Ser
 7075 7080 7085

gtc aag tcc aat gtc ggt cac aca cag gct gcc gcg ggc gtc gcc ggg 21486
 Val Lys Ser Asn Val Gly His Thr Gln Ala Ala Ala Gly Val Ala Gly
 7090 7095 7100

gtg atc aag atg gtg atg gcg ctg cgg aat ggt ctg ctg ccg cgg acg 21534
 Val Ile Lys Met Val Met Ala Leu Arg Asn Gly Leu Leu Pro Arg Thr
 7105 7110 7115

ttg cat gtg gat gag ccg tcg ccg cat gtg gac tgg tcc gcg ggt gcg 21582
 Leu His Val Asp Glu Pro Ser Pro His Val Asp Trp Ser Ala Gly Ala
 7120 7125 7130

gtg cag ctg ctg acg gag acg gtg ccc tgg ccc ggc ggg gag ggg ccg 21630
 Val Gln Leu Leu Thr Glu Thr Val Pro Trp Pro Gly Gly Glu Gly Arg
 7135 7140 7145 7150

cta cgg cgg gca gga gtg tca tca ttc ggc gtc agc ggc acc aac gcc 21678
 Leu Arg Arg Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala
 7155 7160 7165

cac gtc atc ctc gaa gaa gca ccc gcc cac aac atc ccg tca gac aca 21726
 His Val Ile Leu Glu Glu Ala Pro Ala His Asn Ile Pro Ser Asp Thr

7170

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ccc gcc gac gac gtt ccg ggg gga cca ccc gcc ggc gag gat gcc ggt 21774
 Pro Ala Asp Asp Val Pro Gly Gly Pro Pro Ala Gly Glu Asp Ala Gly

7185

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7195

agt ggc gag gag gct gct gcc ggc agt cca ggg gtg tgg ccg tgg ctg 21822
 Ser Gly Glu Glu Ala Ala Ala Gly Ser Pro Gly Val Trp Pro Trp Leu

7200

7205

7210

gtg tcg gcc aag tcg cag ccg gcc ctg cgc gcc cag gcc cag gcc ctg 21870
 Val Ser Ala Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln Ala Leu

7215

7220

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cac gcc cac ctc acc gac cac ccc ggc ctc gac ctc gcc gac gtc gga 21918
 His Ala His Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp Val Gly

7235

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7245

tac acc ctc gcc cac gcc cgc gcc gtg ttc gac cac cgc gcc acc ctc 21966
 Tyr Thr Leu Ala His Ala Arg Ala Val Phe Asp His Arg Ala Thr Leu

7250

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atc gcc gcc gac cgc gac acc ttc ctg caa gca ctc cag gca ctc gcc 22014
 Ile Ala Ala Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala Leu Ala

7265

7270

7275

gca ggc gaa ccc cac ccc gcc gtc atc cac agc agc gcc cca ggc ggg 22062
 Ala Gly Glu Pro His Pro Ala Val Ile His Ser Ser Ala Pro Gly Gly

7280

7285

7290

acc ggg acc ggg gag gcc gca gga aag acc gca ttc atc tgc tcc gga 22110
 Thr Gly Thr Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys Ser Gly

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7300

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cag ggc acc caa cgc ccc ggc atg gcc cac ggc ctc tac cac acc cac 22158
 Gln Gly Thr Gln Arg Pro Gly Met Ala His Gly Leu Tyr His Thr His

7315

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ccc gtc ttc gcc gcc gca ctc aac gac atc tgc acc cac ctc gac ccc 22206
 Pro Val Phe Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu Asp Pro
 7330 7335 7340

cac ctc gac cac ccc ctc ctc ccc ctc ctc acc cag gac ccc aac acc 22254
 His Leu Asp His Pro Leu Leu Pro Leu Leu Thr Gln Asp Pro Asn Thr
 7345 7350 7355

cag gac acc acc acc ctc gaa gaa gcg gcc gca ctg ctc cag cag acc 22302
 Gln Asp Thr Thr Thr Leu Glu Glu Ala Ala Ala Leu Leu Gln Gln Thr
 7360 7365 7370

cgc tac gcc cag ccc gcc ctc ttc gcc ttc cag gtc gcc ctc cac cgc 22350
 Pro Tyr Ala Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg
 7375 7380 7385 7390

ctc ctc acc gac ggc tac cac atc acc ccc cac tac tac gcc gga cac 22398
 Leu Leu Thr Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His
 7395 7400 7405

tcc ctc ggc gaa atc acc gcc gcc cac ctc gcc ggc atc ctc acc ctc 22446
 Ser Leu Gly Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu
 7410 7415 7420

acc gac gcc acc acc ctc atc acc caa cgc gcc acc ctc atg caa acc 22494
 Thr Asp Ala Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr
 7425 7430 7435

atg ccc ccc ggc acc atg acc acc ctc cac acc acc ccc cac cac atc 22542
 Met Pro Pro Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile
 7440 7445 7450

acc cac cac atc acc gcc cac gaa aac gac ctc gcc atc gcc gcc atc 22590
 Thr His His Ile Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile
 7455 7460 7465 7470

aac acc ccc acc tcc ctc gtc atc agc ggc acc ccc cac acc gtc caa 22638
 Asn Thr Pro Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln

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cac atc acc acc ctc tgc caa caa caa ggc atc aaa acc aaa acc ctc 22686
His Ile Thr Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu

7490

7495

7500

ccc acc aac cac gcc ttc cac tcc ccc cac acc aac ccc atc ctc aac 22734
Pro Thr Asn His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn

7505

7510

7515

caa ctc cac cag cac acc caa acc ctc acc tac cac cca ccc cac acc 22782
Gln Leu His Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr

7520

7525

7530

ccc ctc atc acc gcc aac acc cca ccc gac caa ctc ctc acc ccc cac 22830
Pro Leu Ile Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His

7535

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7545

7550

tac tgg acc caa caa gcc cgc aac acc gtc gac ata gcc acc acc acc 22878
Tyr Trp Thr Gln Gln Ala Arg Asn Thr Val Asp Ile Ala Thr Thr Thr

7555

7560

7565

caa acc ctc cac caa cac ggc gtc acc acc tac atc gaa ctc gga ccc 22926
Gln Thr Leu His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro

7570

7575

7580

gac aac acc ctc acc acc ctc acc cac cac aac ctc ccc aac acc ccc 22974
Asp Asn Thr Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Thr Pro

7585

7590

7595

acc acc acc ctc acc ctc acc cac ccc cac cac cac ccc caa acc cac 23022
Thr Thr Thr Leu Thr Leu Thr His Pro His His His Pro Gln Thr His

7600

7605

7610

ctc ctc acc aac ctc gcc aaa acc acc acc acc tgg cac ccc cac cac 23070
Leu Leu Thr Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His

7615

7620

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tac acc cac cac cac aac caa ccc cac acc cac acc cac ctc gac ctc 23118
 Tyr Thr His His His Asn Gln Pro His Thr His Thr His Leu Asp Leu
 7635 7640 7645

ccc acc tac ccc ttc caa cac cac cac tac tgg ctc gaa agc aca cag 23166
 Pro Thr Tyr Pro Phe Gln His His His Tyr Trp Leu Glu Ser Thr Gln
 7650 7655 7660

ccc ggt gcc ggc aac gtg tca gca gcc gga ctc gac ccc acc gaa cac 23214
 Pro Gly Ala Gly Asn Val Ser Ala Ala Gly Leu Asp Pro Thr Glu His
 7665 7670 7675

ccc cta ctc ggc gcc aca ttg gaa ctg gcc gaa ggg gac ggc tgc cta 23262
 Pro Leu Leu Gly Ala Thr Leu Glu Leu Ala Glu Gly Asp Gly Cys Leu
 7680 7685 7690

ctg acg ggg cgc ctc tcg ttg cgc acg cat ccc tgg ctc gcc ggc cat 23310
 Leu Thr Gly Arg Leu Ser Leu Arg Thr His Pro Trp Leu Ala Gly His
 7695 7700 7705 7710

gcg gta ggc ggt gtc gtg ctg ctg ccg ggt acg gcc ttc gcg gaa ctg 23358
 Ala Val Gly Gly Val Val Leu Leu Pro Gly Thr Ala Phe Ala Glu Leu
 7715 7720 7725

gcc ctt cat gcc gga gaa agt gtg ggt tgc gac cac gtg gac gag ctg 23406
 Ala Leu His Ala Gly Glu Ser Val Gly Cys Asp His Val Asp Glu Leu
 7730 7735 7740

acg ctc cac aca ccg ttg gtc att cct gag gtc gga gac gtg acc ctt 23454
 Thr Leu His Thr Pro Leu Val Ile Pro Glu Val Gly Asp Val Thr Leu
 7745 7750 7755

cag gtt gcc att gcg gcg ccg gac gag tcg ggt cgc cgc atg atg acc 23502
 Gln Val Ala Ile Ala Ala Pro Asp Glu Ser Gly Arg Arg Met Met Thr
 7760 7765 7770

atc cac tca cgc ggt gag ggc ggc agt ggt gga gcc gat gcg tcg gcc 23550
 Ile His Ser Arg Gly Glu Gly Gly Ser Gly Gly Ala Asp Ala Ser Ala

7775

7780

7785

7790

agt gcg tgg acg cgt cat gcc gcg ggt gtg ctg agc cct gcc aag gac 23598
 Ser Ala Trp Thr Arg His Ala Ala Gly Val Leu Ser Pro Ala Lys Asp

7795

7800

7805

gat gac act gcc tcg tac gag ctg ctt gcg gga ccc tgg cct ccc gtt 23646
 Asp Asp Thr Ala Ser Tyr Glu Leu Leu Ala Gly Pro Trp Pro Pro Val

7810

7815

7820

gga gct acg cct gtc gac ctg aac acg gct tac gat caa atg gcc gac 23694
 Gly Ala Thr Pro Val Asp Leu Asn Thr Ala Tyr Asp Gln Met Ala Asp

7825

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7835

gcc ggc ttt gct tat ggc ctg gca ttc caa ggg ttg cgc gcg gcc tgg 23742
 Ala Gly Phe Ala Tyr Gly Leu Ala Phe Gln Gly Leu Arg Ala Ala Trp

7840

7845

7850

cgc tac ggc gac gac atc ctc gtc gag gca cgt ctt ccc gaa gaa gtg 23790
 Arg Tyr Gly Asp Asp Ile Leu Val Glu Ala Arg Leu Pro Glu Glu Val

7855

7860

7865

7870

tcg gga gac gcg gcg gcg tac ggt ctg cac ccg gcc ctg ctc gac gct 23838
 Ser Gly Asp Ala Ala Ala Tyr Gly Leu His Pro Ala Leu Leu Asp Ala

7875

7880

7885

gcc ctt cag ggc acc ggc ctg ctt tct gtg gcg ggt ccg ggg acg ccc 23886
 Ala Leu Gln Gly Thr Gly Leu Leu Ser Val Ala Gly Pro Gly Thr Pro

7890

7895

7900

gtc gtg ccc cat gtg tgg aac ggt ctg cgg ttc cgt acg cat ggt gca 23934
 Val Val Pro His Val Trp Asn Gly Leu Arg Phe Arg Thr His Gly Ala

7905

7910

7915

gtc tcc gtg cgc gcg tgc ctg tcg acg ctt gga gcg aca ggg gcg gcc 23982
 Val Ser Val Arg Ala Cys Leu Ser Thr Leu Gly Ala Thr Gly Ala Ala

7920

7925

7930

gtg tgc gtg cgc atc acc gac gac acc ggg gtg ccg gtg gcg tgc gtc 24030
 Val Cys Val Arg Ile Thr Asp Asp Thr Gly Val Pro Val Ala Ser Val
 7935 7940 7945 7950

gat cgt ctt gag ttg cgg cct gtg gat atg ggt cag ttg cgt gct gtc 24078
 Asp Arg Leu Glu Leu Arg Pro Val Asp Met Gly Gln Leu Arg Ala Val
 7955 7960 7965

tcg gtt tcg gcg ggg cgg cgg ggt tcg ctg tat gcg gtg cag tgg gct 24126
 Ser Val Ser Ala Gly Arg Arg Gly Ser Leu Tyr Ala Val Gln Trp Ala
 7970 7975 7980

gag gtg ggt cct gtg ccg gtg tgt ggg cag gcg tgg gcg tgg cac gag 24174
 Glu Val Gly Pro Val Pro Val Cys Gly Gln Ala Trp Ala Trp His Glu
 7985 7990 7995

gac gtg ggt gag agc ggt ggt ggg cct gtg ccg ggg gtg gtg gtg ttg 24222
 Asp Val Gly Glu Ser Gly Gly Gly Pro Val Pro Gly Val Val Val Leu
 8000 8005 8010

cgg tgc ccg gat gcc ggt gcc gat ggc ggc ggt ggc ggt ggt gtg ggt 24270
 Arg Cys Pro Asp Ala Gly Ala Asp Gly Gly Gly Gly Gly Gly Val Gly
 8015 8020 8025 8030

gag gtt gtt ggt ggg gtg ttg ggt gtg gtg cag ggg tgg ctg ggg ctg 24318
 Glu Val Val Gly Gly Val Leu Gly Val Val Gln Gly Trp Leu Gly Leu
 8035 8040 8045

gag cgg ttt gcg ggt tcg cgg ctg gtg gtg gtg acc cgg ggt gcg gtg 24366
 Glu Arg Phe Ala Gly Ser Arg Leu Val Val Val Thr Arg Gly Ala Val
 8050 8055 8060

gtg gcc ggc ccg gag gac ggc ccg gtg gat gtg gtg ggt gcg gcg gtg 24414
 Val Ala Gly Pro Glu Asp Gly Pro Val Asp Val Val Gly Ala Ala Val
 8065 8070 8075

tgg ggg ctg gtg cgg tcg gcg cag gct gag cat ccg gac cgg ttt gtc 24462
 Trp Gly Leu Val Arg Ser Ala Gln Ala Glu His Pro Asp Arg Phe Val

8080

8085

8090

ctc ctc gac ctg gac acc gac ctc gac agc ggc gct gac gcc gat gcc 24510
 Leu Leu Asp Leu Asp Thr Asp Leu Asp Ser Gly Ala Asp Ala Asp Ala
 8095 8100 8105 8110

ggc aac gag gcc ggt atg ggg tct ggt ctg gat ggt ggg cgt gtg gct 24558
 Gly Asn Glu Ala Gly Met Gly Ser Gly Leu Asp Gly Gly Arg Val Ala
 8115 8120 8125

gcg gtg gtg gcg tgt ggt gag ccg cag ttg gcg gtg cgt ggt gag cgg 24606
 Ala Val Val Ala Cys Gly Glu Pro Gln Leu Ala Val Arg Gly Glu Arg
 8130 8135 8140

gtg ctg gcc gca cgc ctg aca cga ctt gag tcg ccg gtt gat gta tcg 24654
 Val Leu Ala Ala Arg Leu Thr Arg Leu Glu Ser Pro Val Asp Val Ser
 8145 8150 8155

ggt cgg gag gtg ttg ccg tgg ttg tcg ggt ggg tcg gtg ttg gtg acg 24702
 Gly Arg Glu Val Leu Pro Trp Leu Ser Gly Gly Ser Val Leu Val Thr
 8160 8165 8170

ggt ggg acg ggt gtg ctg ggt gcg gcg gtg gcg cgg cat ctg gct ggt 24750
 Gly Gly Thr Gly Val Leu Gly Ala Ala Val Ala Arg His Leu Ala Gly
 8175 8180 8185 8190

gtg tgt ggg gtg cgg gat ctg ttg ttg gtg agc cgg cgt ggt ccg gat 24798
 Val Cys Gly Val Arg Asp Leu Leu Leu Val Ser Arg Arg Gly Pro Asp
 8195 8200 8205

gct ccg ggt gcg gag ggt ttg cgg gcg gag ctg gcc gcg ttg ggg gcg 24846
 Ala Pro Gly Ala Glu Gly Leu Arg Ala Glu Leu Ala Ala Leu Gly Ala
 8210 8215 8220

gag gtg cgg att gtt gcg tgt gat gtg ggg gag cgg cgg gag gtg gtc 24894
 Glu Val Arg Ile Val Ala Cys Asp Val Gly Glu Arg Arg Glu Val Val
 8225 8230 8235

cgg ctg ctg gag ggt gtt cct gcc ggg tgt ccg ctg acg ggt gtc gtg 24942
 Arg Leu Leu Glu Gly Val Pro Ala Gly Cys Pro Leu Thr Gly Val Val
 8240 8245 8250

cat gcg gct ggt gtg ctg gac gat gcg acg atc gcc tct ctc acg ccc 24990
 His Ala Ala Gly Val Leu Asp Asp Ala Thr Ile Ala Ser Leu Thr Pro
 8255 8260 8265 8270

gag cgg ctg ggc acg gtg ttc gcg gcc aag gtg gat gcc gct ctt ttg 25038
 Glu Arg Leu Gly Thr Val Phe Ala Ala Lys Val Asp Ala Ala Leu Leu
 8275 8280 8285

ctg gat gag ctg acg cgg ggt atg gag ctg tcg gcg ttc gtg ctg ttc 25086
 Leu Asp Glu Leu Thr Arg Gly Met Glu Leu Ser Ala Phe Val Leu Phe
 8290 8295 8300

tcc tcg gcc gcg ggg atc ctg ggg tcg gcc ggg cag ggc aac tac gcc 25134
 Ser Ser Ala Ala Gly Ile Leu Gly Ser Ala Gly Gln Gly Asn Tyr Ala
 8305 8310 8315

gcg gcc aat gcc gct ctg gac gcg ctg gcg tac cgg cgg cgg gcg gcg 25182
 Ala Ala Asn Ala Ala Leu Asp Ala Leu Ala Tyr Arg Arg Arg Ala Ala
 8320 8325 8330

ggt ctg ccg ggg gtg tcg ctg gcg tgg ggg ctg tgg gaa gag gcc agc 25230
 Gly Leu Pro Gly Val Ser Leu Ala Trp Gly Leu Trp Glu Glu Ala Ser
 8335 8340 8345 8350

ggg atg acc ggg cac ctg gcc ggc acc gac cac cgg cgc atc atc cgt 25278
 Gly Met Thr Gly His Leu Ala Gly Thr Asp His Arg Arg Ile Ile Arg
 8355 8360 8365

tcc ggt ctg cat ccc atg tcg acc ccg gac gca ctg gct ctc ttc gat 25326
 Ser Gly Leu His Pro Met Ser Thr Pro Asp Ala Leu Ala Leu Phe Asp
 8370 8375 8380

gcg gcc ctg gct ctg gac cgg ccg gtc ctg ctg ccc gcc gac ctg cgt 25374
 Ala Ala Leu Ala Leu Asp Arg Pro Val Leu Leu Pro Ala Asp Leu Arg

8385	8390	8395	
ccc gcc ccg ccc ctg ccg ccc ctg ctg cag gac ctc ctg ccc gcc acc			25422
Pro Ala Pro Pro Leu Pro Pro Leu Leu Gln Asp Leu Leu Pro Ala Thr			
8400	8405	8410	
cgc cgc cgc acc acc cgc acc acc act acc ggt ggt gcg gac aac ggc			25470
Arg Arg Arg Thr Thr Arg Thr Thr Thr Thr Gly Gly Ala Asp Asn Gly			
8415	8420	8425	8430
gcc cag ctg cat gcc cgg ctg gcc ggc cag aca cac gaa caa cag cac			25518
Ala Gln Leu His Ala Arg Leu Ala Gly Gln Thr His Glu Gln Gln His			
8435	8440	8445	
acc acc ctc ctc gcc ctg gtc cgc tcc cac atc gcc acc gtc ctc ggc			25566
Thr Thr Leu Leu Ala Leu Val Arg Ser His Ile Ala Thr Val Leu Gly			
8450	8455	8460	
cac aac gcg ccg gag atg atc ccc gtt gac tcg gcg ttc cgc gac cta			25614
His Asn Ala Pro Glu Met Ile Pro Val Asp Ser Ala Phe Arg Asp Leu			
8465	8470	8475	
ggc ttc gac tcc ttg aca gcg gtg gaa ctc cgt aac cgc ctg ggt gag			25662
Gly Phe Asp Ser Leu Thr Ala Val Glu Leu Arg Asn Arg Leu Gly Glu			
8480	8485	8490	
gca acg gga ctg cga ctg ccg acc agt ctg gtc ttc gac cag ccg aat			25710
Ala Thr Gly Leu Arg Leu Pro Thr Ser Leu Val Phe Asp Gln Pro Asn			
8495	8500	8505	8510
gca gcg acc ctg gcg cgt cac cta cgt cgt gag ctg atg ggc gac gac			25758
Ala Ala Thr Leu Ala Arg His Leu Arg Arg Glu Leu Met Gly Asp Asp			
8515	8520	8525	
gcg gaa ggc gag acg cca tcg cag gtc gca ctt cat cag gtt gcc gcg			25806
Ala Glu Gly Glu Thr Pro Ser Gln Val Ala Leu His Gln Val Ala Ala			
8530	8535	8540	

gat gag ccg att gcg att gtg ggg atg gcg tgt cgt ttt ccg ggt ggg 25854
 Asp Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Phe Pro Gly Gly
 8545 8550 8555

gtg tgt tcg ccg gag gag ttg tgg gag ctg gtt gcg tcg ggt ggg gat 25902
 Val Cys Ser Pro Glu Glu Leu Trp Glu Leu Val Ala Ser Gly Gly Asp
 8560 8565 8570

gcg att ggt gaa ttt ccg gcc ggt cgg ggg tgg gat ctg gag ggg ttg 25950
 Ala Ile Gly Glu Phe Pro Ala Gly Arg Gly Trp Asp Leu Glu Gly Leu
 8575 8580 8585 8590

ttt gat tcg gac cct gac cgg tcg ggg acg tcg tac gcg cgg tat ggc 25998
 Phe Asp Ser Asp Pro Asp Arg Ser Gly Thr Ser Tyr Ala Arg Tyr Gly
 8595 8600 8605

ggg ttt ttg tat gag gcg ggg gag ttc gat gcg gac ttc ttc ggg atc 26046
 Gly Phe Leu Tyr Glu Ala Gly Glu Phe Asp Ala Asp Phe Phe Gly Ile
 8610 8615 8620

agt ccg cgt gag gcg ttg gcg atg gat ccg cag cag cgg ttg ttg ctg 26094
 Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu
 8625 8630 8635

gag acg tcg tgg gag gcg ttc gag cgg gcg ggt atc gat ccg ctg tcg 26142
 Glu Thr Ser Trp Glu Ala Phe Glu Arg Ala Gly Ile Asp Pro Leu Ser
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 Met Arg Gly Ser Arg Thr Gly Val Phe Ala Gly Val Met Tyr His Asp
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 Tyr Ala Ala Arg Leu His His Val Pro Glu Gly Phe Glu Gly Leu Ile
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8770

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Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly

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9045

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9065

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9080

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9095

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9105

9110

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Ser Gln Gly Glu Ile Ala Ala Ala His Ile Cys Gly Ala Leu Ser Leu
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Lys Asp Ala Ala Lys Thr Val Ala Leu Arg Ser Gln Ala Leu Ala Ala
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Val Arg Gly Arg Gly Ala Met Val Ser Leu Pro Leu Pro Ala Gln Asp
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Ala Leu Asn Gly Pro His Ser Thr Thr Val Ser Gly Asp Thr Thr Ala
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Val Glu Glu Leu Leu Thr His Cys Ala Asp Thr Gly Leu Arg Ala Lys
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His Asp Glu Leu Leu His Leu Leu Gly Asp Ile Thr Pro Gln Pro Ser

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9305

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Ala Thr Leu Thr Leu Ala Asn Asn Asn Thr Gln Leu Leu Thr Gly Arg	
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ctc tcc cta cgc acc cac ccc tgg ctc acc gac cac acc gtc gtc ggt	28686
Leu Ser Leu Arg Thr His Pro Trp Leu Thr Asp His Thr Val Val Gly	
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Thr Lys Thr Ser Arg Ile Glu Thr Gly Arg Ser His Asp Asp Leu Ser	
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Met Trp Pro Pro Ala Gly Ala Val Arg Cys Ala Asp Glu Glu Leu Ala	

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 Phe Arg Gly Leu Thr Ala Ala Trp Arg Leu Gly Asp Glu Val Phe Ala
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 Leu His Pro Ala Leu Leu Asp Ala Ala Leu His Ala Ala Ala Phe Ala
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Ala Pro Tyr Val Asp Trp Ser Val Glu Gln Val Leu Arg Asp Ser Pro
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Ala Val Met Ile Ser Leu Ala Ala Leu Trp Arg Ser Gln Gly Val Glu

100

105

110

Pro Cys Ala Val Leu Gly His Ser Leu Gly Glu Ile Ala Ala Ala His
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Val Ala Ala Thr Pro Asp Glu Leu Leu Pro Arg Ile Ala Pro Trp Thr
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Ser Thr Val Val Ser Gly Ala Arg Glu Ala Val Ala Asp Leu Val Ala
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Pro Ala His Ser Pro Leu Met Tyr Ala Ile Glu Glu Arg Val Val Ser
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Ser Val Thr Gly Gly Arg Leu Asp Thr Arg Glu Leu Asp Ala Ala Tyr
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Trp Tyr Arg Asn Met Ser Ser Thr Val Arg Phe Glu Pro Ala Ala Arg
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Pro Val Leu Thr Met Gly Leu Gln Glu Leu Ala Pro Asp Leu Gly Asp
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Thr Thr Gly Thr Ala Asp Thr Val Ile Met Gly Thr Leu Arg Arg Gly
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Gln Gly Thr Leu Asp His Phe Leu Thr Ser Leu Ala Gln Leu Arg Gly
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Arg Ser Pro Lys Asp Leu Trp Glu Leu Ala Ala Ser Gly Gly Asp Ala
500 505 510

Ile Gly Pro Phe Pro Thr Asp Arg Gly Trp Pro Thr Glu Gln Arg His
515 520 525

Ala Gln Asp Pro Thr Gln Pro Gly Thr Phe Tyr Pro Gln Gly Gly Gly
530 535 540

Phe Leu His Asp Ala Ala His Phe Asp Ala Gly Phe Phe Gly Ile Ser
545 550 555 560

Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu
565 570 575

Thr Ser Trp Glu Ala Phe Glu Arg Ala Gly Ile Asp Pro Leu Ser Val
580 585 590

Arg Gly Ser Arg Thr Gly Val Phe Ala Gly Ala Leu Ser Phe Asp Tyr
595 600 605

Gly Pro Arg Met Asp Thr Ala Ser Ser Glu Gly Ala Ala Asp Val Glu
610 615 620

Gly His Ile Leu Thr Gly Thr Thr Gly Ser Val Leu Ser Gly Arg Ile
625 630 635 640

Ala Tyr Ser Phe Gly Leu Glu Gly Pro Ala Ile Thr Val Asp Thr Gly
645 650 655

Cys Ser Ala Ser Leu Val Thr Leu His Leu Ala Cys Gln Ser Leu Arg
660 665 670

Ser Gly Glu Cys Thr Leu Ala Leu Ala Gly Gly Val Ser Val Met Ser
675 680 685

Thr Leu Gly Met Phe Ile Glu Phe Ser Arg Gln Arg Gly Leu Ser Val
690 695 700

Asp Gly Arg Cys Lys Ala Tyr Ser Ala Ala Ala Asp Gly Thr Gly Trp

705

710

715

720

Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Val

725

730

735

Arg Leu Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn

740

745

750

Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ala Gln

755

760

765

Glu Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Ser Val Ala

770

775

780

Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly Asp

785

790

795

800

Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Arg Ala Gly

805

810

815

Asp Arg Pro Leu Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Thr

820

825

830

Met Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala Leu

835

840

845

Arg Glu Gly Val Leu Pro Arg Thr Leu His Val Asp Lys Pro Ser Pro

850

855

860

Gln Val Asp Trp Ser Ala Gly Ala Val Arg Leu Leu Thr Glu Ala Val

865

870

875

880

Pro Trp Pro Gly Asp Ala Ala Gly Arg Leu Arg Arg Ala Gly Val Ser

885

890

895

Ser Phe Gly Ile Gly Gly Thr Asn Ala His Val Ile Leu Glu Glu Ala

900

905

910

Pro Ala Ala Gly Gly Cys Val Ala Gly Gly Gly Val Leu Glu Gly Ala
915 920 925

Pro Gly Leu Ala Ile Ser Val Ala Glu Ser Val Ala Ala Pro Val Ala
930 935 940

Val Ser Ala Pro Val Ala Glu Ser Val Pro Val Pro Val Pro Val Pro
945 950 955 960

Val Pro Val Pro Val Ser Ala Arg Ser Glu Ala Gly Leu Arg Ala Gln
965 970 975

Ala Glu Ala Leu Arg Gln Tyr Val Ala Val Arg Pro Asp Val Ser Leu
980 985 990

Ala Asp Val Gly Ala Gly Leu Ala Cys Gly Arg Ala Val Leu Glu His
995 1000 1005

Arg Ala Val Val Leu Ala Ala Asp Arg Glu Glu Leu Val Gln Gly Leu
1010 1015 1020

Gly Ala Leu Ala Ala Gly Glu Pro Asp Arg Arg Val Thr Thr Gly His
1025 1030 1035 1040

Ala Pro Gly Gly Asp Arg Gly Gly Val Val Phe Val Phe Pro Gly Gln
1045 1050 1055

Gly Gly Gln Trp Ala Gly Met Gly Val Arg Leu Leu Ala Ser Ser Pro
1060 1065 1070

Val Phe Ala Arg Arg Met Gln Ala Cys Glu Glu Ala Leu Ala Pro Trp
1075 1080 1085

Val Asp Trp Ser Val Val Asp Ile Leu Arg Arg Asp Ala Gly Asp Ala
1090 1095 1100

Val Trp Glu Arg Ala Asp Val Val Gln Pro Val Leu Phe Ser Val Met
1105 1110 1115 1120

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Val Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Ile Glu Pro Asp Ala
1125 1130 1135

Val Leu Gly His Ser Gln Gly Glu Ile Ala Ala Ala His Val Cys Gly
1140 1145 1150

Ala Leu Ser Leu Lys Asp Ala Ala Lys Thr Val Ala Leu Arg Ser Arg
1155 1160 1165

Ala Leu Ala Ala Val Arg Gly Arg Gly Gly Met Ala Ser Val Pro Leu
1170 1175 1180

Pro Ala Gln Glu Val Glu Gln Leu Ile Gly Glu Arg Trp Ala Gly Arg
1185 1190 1195 1200

Leu Trp Val Ala Ala Val Asn Gly Pro Arg Ser Thr Ala Val Ser Gly
1205 1210 1215

Asp Ala Glu Ala Val Asp Glu Val Leu Ala Tyr Cys Ala Gly Thr Gly
1220 1225 1230

Val Arg Ala Arg Arg Ile Pro Val Asp Tyr Ala Ser His Cys Pro His
1235 1240 1245

Val Gln Pro Leu Arg Glu Glu Leu Leu Glu Leu Leu Gly Asp Ile Ser
1250 1255 1260

Pro Gln Pro Ser Gly Val Pro Phe Phe Ser Thr Val Glu Gly Thr Trp
1265 1270 1275 1280

Leu Asp Thr Thr Thr Leu Asp Ala Ala Tyr Trp Tyr Arg Asn Leu His
1285 1290 1295

Gln Pro Val Arg Phe Ser Asp Ala Val Gln Ala Leu Ala Asp Asp Gly
1300 1305 1310

His Arg Val Phe Val Glu Val Ser Pro His Pro Thr Leu Val Pro Ala

1315

1320

1325

Ile Glu Asp Thr Thr Glu Asp Thr Ala Glu Asp Val Thr Ala Ile Gly
 1330 1335 1340

Ser Leu Arg Arg Gly Asp Asn Asp Thr Arg Arg Phe Leu Thr Ala Leu
 1345 1350 1355 1360

Ala His Thr His Thr Thr Gly Ile Gly Thr Pro Thr Thr Trp His His
 1365 1370 1375

His Tyr Thr His His His Thr His Pro His Pro His Thr His Leu Asp
 1380 1385 1390

Leu Pro Thr Tyr Pro Phe Gln His Gln His Tyr Trp Leu Glu Ser Ser
 1395 1400 1405

Gln Pro Gly Ala Gly Ser Gly Ser Gly Ala Gly Ala Gly Ser Gly Ala
 1410 1415 1420

Gly Ser Gly Arg Ala Gly Thr Ala Gly Gly Thr Ala Glu Val Glu Ser
 1425 1430 1435 1440

Arg Phe Trp Asp Ala Val Ala Arg Gln Asp Leu Glu Thr Val Ala Thr
 1445 1450 1455

Thr Leu Ala Val Pro Pro Ser Ala Gly Leu Asp Thr Val Val Pro Ala
 1460 1465 1470

Leu Ser Ala Trp His Arg His Gln His Asp Gln Ala Arg Ile Asn Thr
 1475 1480 1485

Trp Thr Tyr Gln Glu Thr Trp Lys Pro Leu Thr Leu Pro Thr Thr His
 1490 1495 1500

Gln Pro His Gln Thr Trp Leu Ile Ala Ile Pro Glu Thr Gln Thr His
 1505 1510 1515 1520

His Pro His Ile Thr Asn Ile Leu Thr Asn Leu His His His Gly Ile
 1525 1530 1535

Thr Pro Ile Pro Leu Thr Leu Asn His Thr His Thr Asn Pro Gln His
 1540 1545 1550

Leu His His Thr Leu His His Thr Arg Gln Gln Ala Gln Asn His Thr
 1555 1560 1565

Thr Gly Ala Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu Asp Glu Thr
 1570 1575 1580

Pro His Pro His His Pro His Thr Pro Thr Gly Thr Leu Leu Asn Leu
 1585 1590 1595 1600

Thr Leu Thr Gln Thr His Thr Gln Thr His Pro Pro Thr Pro Leu Trp
 1605 1610 1615

Tyr Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp Pro Leu Thr
 1620 1625 1630

His Pro Thr Gln Ala Gln Thr Trp Gly Leu Ala Arg Thr Thr Leu Leu
 1635 1640 1645

Glu His Pro Thr His Thr Ala Gly Ile Ile Asp Leu Pro Thr Thr Pro
 1650 1655 1660

Thr Pro His Thr Leu Gln His Leu Thr Gln Thr Leu Thr Gln Pro His
 1665 1670 1675 1680

His Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His Thr Arg Arg
 1685 1690 1695

Leu Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro Thr Pro Thr
 1700 1705 1710

Pro His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala Leu Ala Thr
 1715 1720 1725

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His Leu Thr His His Leu Thr Thr His Gln Pro Thr Gln His Leu Leu
1730 1735 1740

Leu Thr Ser Arg Thr Gly Pro His Thr Pro His Ala Gln His Leu Thr
1745 1750 1755 1760

Thr Gln Leu Gln Gln Lys Gly Ile His Leu Thr Ile Thr Thr Cys Asp
1765 1770 1775

Thr Ser Asn Pro Asp Gln Leu Gln Gln Leu Leu Asn Thr Ile Pro Pro
1780 1785 1790

Gln His Pro Leu Thr Thr Val Ile His Thr Ala Gly Ile Leu Asp Asp
1795 1800 1805

Ala Thr Leu Thr Asn Leu Thr Pro Thr Gln Leu Asn Asn Val Leu Arg
1810 1815 1820

Ala Lys Ala His Ser Ala His Leu Leu His Gln Leu Thr Gln His Thr
1825 1830 1835 1840

Pro Leu Thr Ala Phe Val Leu Tyr Ser Ser Ala Ala Ala Thr Phe Gly
1845 1850 1855

Ala Pro Gly Gln Ala Asn Tyr Ala Ala Ala Asn Ala Tyr Leu Asp Ala
1860 1865 1870

Leu Ala His His Arg His Thr His His Leu Pro Ala Thr Ser Ile Ala
1875 1880 1885

Trp Gly Thr Trp Gln Gly Asn Gly Leu Ala Asp Ser Asp Lys Ala Arg
1890 1895 1900

Ala Tyr Leu Asp Arg Arg Gly Phe Arg Pro Met Ser Pro Glu Leu Ala
1905 1910 1915 1920

Thr Ala Ala Val Thr Gln Ala Ile Ala Asp Thr Glu Arg Pro Tyr Val

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T04200 9924T650

1925	1930	1935
Val Ile Ala Asp Ile Asp Trp Ser Lys Ile Glu His Thr Ser Gln Thr		
1940	1945	1950
Ser Asp Leu Val Ser Ala Ala Arg Glu Arg Glu Pro Ala Val Gln Arg		
1955	1960	1965
Pro Thr Pro Pro Ala Glu Leu His Lys Thr Leu Ala His Gln Thr Ser		
1970	1975	1980
Ala Asp Gln Arg Ala Ala Leu Leu Glu Leu Val Arg Asp His Val Ala		
1985	1990	1995 2000
Ala Val Leu Arg His Ala Asp Pro Lys Ala Ile Ala Pro Asp Gln Ser		
2005	2010	2015
Phe Arg Ala Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Phe Arg Asn		
2020	2025	2030
Leu Leu Ile Lys Ala Thr Gly Leu Arg Leu Pro Val Ser Leu Val Phe		
2035	2040	2045
Asp His Pro Thr Pro Ala Lys Leu Ala Val His Leu Gln Asn Gln Leu		
2050	2055	2060
Arg Gly Thr Ala Ala Glu Ser Ala Pro Ser Ala Ala Ala Val Thr Ala		
2065	2070	2075 2080
Glu Ala Ser Val Thr Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg		
2085	2090	2095
Phe Pro Gly Gly Val Thr Ser Ala Asp Asp Phe Trp Asp Leu Ile Ser		
2100	2105	2110
Ser Glu Gln Asp Ala Ile Gly Gly Phe Pro Thr Asp Arg Gly Trp Asp		
2115	2120	2125

Leu Asp Thr Leu Tyr Asp Pro Asp Pro Asp His Pro Gly Thr Cys Tyr
 2130 2135 2140

Thr Arg Asn Gly Gly Phe Leu Tyr Asp Ala Gly His Phe Asp Ala Glu
 2145 2150 2155 2160

Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln
 2165 2170 2175

Arg Leu Leu Leu Glu Thr Ala Trp Glu Thr Ile Glu His Ala Gly Ile
 2180 2185 2190

Asn Pro His Thr Leu His Gly Thr Pro Thr Gly Val Phe Thr Gly Thr
 2195 2200 2205

Asn Gly Gln Asp Tyr Ala Leu Arg Val His Asn Ala Gly Gln Ser Thr
 2210 2215 2220

Asp Gly Phe Ala Leu Thr Gly Thr Ala Gly Ser Val Ile Ser Gly Arg
 2225 2230 2235 2240

Ile Ser Tyr Thr Phe Gly Phe Glu Gly Pro Ala Val Ser Val Asp Thr
 2245 2250 2255

Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala Leu
 2260 2265 2270

Arg Ala Gly Glu Cys Ser Met Ala Leu Ala Gly Gly Val Thr Val Met
 2275 2280 2285

Ser Ser Pro Gly Ala Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala
 2290 2295 2300

Ala Asp Gly His Cys Lys Ala Phe Ser Ala Ala Ala Asp Gly Thr Gly
 2305 2310 2315 2320

Trp Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala
 2325 2330 2335

His Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val
2340 2345 2350

Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser
2355 2360 2365

Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Ser Ala
2370 2375 2380

Gly Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Thr Leu Gly
2385 2390 2395 2400

Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Asp Arg
2405 2410 2415

Ala Gly Glu Gly Pro Leu Trp Leu Gly Ser Val Lys Ser Asn Val Gly
2420 2425 2430

His Thr Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val Met
2435 2440 2445

Ala Leu Arg His Gly Leu Leu Pro Arg Thr Leu His Val Asp Glu Pro
2450 2455 2460

Ser Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu Leu Thr Glu
2465 2470 2475 2480

Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Leu Arg Arg Ala Gly Val
2485 2490 2495

Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu
2500 2505 2510

Ala Pro Ala Asp Asp Val Pro Gly Gly Pro Pro Ala Gly Glu Gly Asp
2515 2520 2525

Ala Gly Ser Asp Asp Glu Ala Ala Ala Gly Ser Pro Gly Val Trp Pro

2530

2535

2540

Trp Leu Val Ser Ala Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln
 2545 2550 2555 2560

Ala Leu His Ala His Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp
 2565 2570 2575

Val Gly Tyr Thr Leu Ala His Ala Arg Ala Val Phe Asp His Arg Ala
 2580 2585 2590

Thr Leu Ile Ala Ala Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala
 2595 2600 2605

Leu Ala Ala Gly Glu Pro His Pro Ala Val Ile His Ser Ser Ala Pro
 2610 2615 2620

Gly Gly Thr Gly Thr Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys
 2625 2630 2635 2640

Ser Gly Gln Gly Thr Gln Arg Pro Gly Met Ala His Gly Leu Tyr His
 2645 2650 2655

Thr His Pro Val Phe Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu
 2660 2665 2670

Asp Pro His Leu Asp His Pro Leu Leu Pro Leu Leu Thr Gln Asn Asp
 2675 2680 2685

Asn Asp Asn Glu Asp Ala Ala Ala Leu Leu Gln Gln Thr Arg Tyr Ala
 2690 2695 2700

Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr
 2705 2710 2715 2720

Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly
 2725 2730 2735

Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala
2740 2745 2750

Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro
2755 2760 2765

Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His His
2770 2775 2780

Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro
2785 2790 2795 2800

Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr
2805 2810 2815

Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Asn
2820 2825 2830

His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His
2835 2840 2845

Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile
2850 2855 2860

Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr
2865 2870 2875 2880

Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr Leu
2885 2890 2895

His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr
2900 2905 2910

Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Pro Pro Thr Thr Thr
2915 2920 2925

Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu Thr
2930 2935 2940

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Asn Leu Ala Lys Thr Thr Thr Trp His Pro His His Tyr Thr His
 2945 2950 2955 2960

His Asp Asn Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr
 2965 2970 2975

Pro Phe Gln His His His Tyr Trp Leu Glu Ser Thr Gln Pro Gly Ala
 2980 2985 2990

Gly Asn Val Ser Ala Ala Gly Leu Asp Pro Thr Glu His Pro Leu Leu
 2995 3000 3005

Gly Ala Thr Leu Glu Leu Ala Thr Asp Gly Gly Ala Leu Leu Ala Gly
 3010 3015 3020

Arg Leu Ser Leu Arg Ser His Pro Trp Leu Ala Asp His Ala Val Gly
 3025 3030 3035 3040

Gly Thr Val Leu Leu Ser Gly Ala Thr Phe Leu Glu Leu Ala Leu His
 3045 3050 3055

Ala Gly Thr Tyr Val Gly Cys Asp Arg Val Asp Glu Leu Thr Leu His
 3060 3065 3070

Ala Pro Leu Val Val Pro Val Asp Gly Gly Val Ser Val Gln Val Gly
 3075 3080 3085

Val Ala Ala Ala Asp Gly Glu Gly Arg Arg Leu Val Ser Val Tyr Ala
 3090 3095 3100

Arg Gly Gly Ser Ala Cys Gly Gly Gly Gly Ala Ser Gly Gly Val Trp
 3105 3110 3115 3120

Thr Cys His Ala Ser Gly Val Leu Val Glu Ala Ala Ala Gly Gly Val
 3125 3130 3135

Val Val Asp Gly Leu Ala Gly Val Trp Pro Pro Arg Gly Ala Val Ala
 3140 3145 3150

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Val Asp Val Asp Gly Val Arg Asp Arg Leu Ala Gly Ala Gly Cys Val
3155 3160 3165

Leu Gly Pro Val Phe Ser Gly Leu Arg Ala Val Trp Arg Asp Gly Gly
3170 3175 3180

Asp Leu Leu Ala Glu Val Cys Leu Pro Glu Glu Ala Trp Gly Asp Ala
3185 3190 3195 3200

Ala Gly Phe Gly Leu His Pro Ala Leu Leu Asp Gly Val Val Gln Pro
3205 3210 3215

Leu Ser Val Leu Leu Pro Gly Gly Thr Gly Phe Gly Glu Gly Ala Gly
3220 3225 3230

Phe Gly Glu Gly Val Arg Val Pro Ala Val Trp Gly Gly Val Ser Leu
3235 3240 3245

His Arg Ala Gly Val Thr Gly Val Arg Val Arg Val Ser Ala Val Gly
3250 3255 3260

Arg Gly Gly Gly Arg Glu Ala Val Ser Val Val Val Gly Asp Glu Ala
3265 3270 3275 3280

Gly Val Pro Val Ala Ser Val Asp Arg Leu Glu Leu Arg Pro Val Asp
3285 3290 3295

Met Gly Gln Leu Arg Ala Val Ser Val Ser Ala Gly Arg Arg Gly Ser
3300 3305 3310

Leu Tyr Ala Val Gln Trp Ala Glu Val Gly Pro Val Pro Val Cys Gly
3315 3320 3325

Gln Ala Trp Ala Trp His Glu Asp Val Gly Glu Ser Gly Gly Gly Pro
3330 3335 3340

Val Pro Gly Val Val Val Leu Arg Cys Pro Asp Ala Gly Ala Gly Gly

3345 3350 3355 3360

Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Val Gly Glu Val Val Gly Gly
3365 3370 3375

Val Leu Gly Val Val Gln Gly Trp Leu Gly Leu Glu Arg Phe Ala Gly
3380 3385 3390

Ser Arg Leu Val Val Val Thr Arg Gly Ala Val Val Ala Gly Pro Glu
3395 3400 3405

Asp Gly Pro Val Asp Val Val Gly Ala Ser Val Trp Gly Leu Val Arg
3410 3415 3420

Ser Ala Gln Ala Glu His Pro Asp Arg Phe Val Leu Leu Asp Leu Asp
3425 3430 3435 3440

Thr Asp Thr Gly Thr Asp Leu Asp Thr Gly Ala Gly Ala Gly Trp Gly
3445 3450 3455

Val Asp Gly Gly Arg Val Ala Ala Val Val Ala Cys Gly Glu Pro Gln
3460 3465 3470

Leu Ala Val Arg Gly Glu Arg Leu Leu Ala Ala Arg Leu Lys Arg Leu
3475 3480 3485

Glu Ser Ser Gly Asp Val Pro Ala Gln Arg Ser Gly Asp Thr Arg Ala
3490 3495 3500

Arg Arg Ser Asp Val Pro Ala Gln Arg Ser Gly Gly Val Pro Ala Arg
3505 3510 3515 3520

Arg Ser Val Asp Val Ser Gly Arg Glu Val Leu Pro Trp Leu Ser Gly
3525 3530 3535

Gly Ser Val Leu Val Thr Gly Gly Thr Gly Val Leu Gly Ala Ala Val
3540 3545 3550

Ala Arg His Leu Ala Gly Val Cys Gly Val Arg Asp Leu Leu Leu Val
 3555 3560 3565

Ser Arg Arg Gly Pro Asp Ala Pro Gly Ala Glu Gly Leu Arg Ala Glu
 3570 3575 3580

Leu Ala Ala Leu Gly Ala Glu Val Arg Ile Val Ala Cys Asp Val Gly
 3585 3590 3595 3600

Glu Arg Arg Glu Val Val Arg Leu Leu Glu Gly Val Pro Ala Gly Cys
 3605 3610 3615

Pro Leu Thr Gly Val Val His Ala Ala Gly Val Leu Asp Asp Ala Thr
 3620 3625 3630

Ile Ala Ser Leu Thr Pro Glu Arg Leu Gly Thr Val Phe Ala Ala Lys
 3635 3640 3645

Val Asp Ala Ala Leu Leu Leu Asp Glu Leu Thr Arg Gly Met Glu Leu
 3650 3655 3660

Ser Ala Phe Val Leu Phe Ser Ser Ala Ala Gly Ile Leu Gly Ser Ala
 3665 3670 3675 3680

Gly Gln Gly Asn Tyr Ala Ala Ala Asn Ala Ala Leu Asp Ala Leu Ala
 3685 3690 3695

Tyr Arg Arg Arg Ala Ala Gly Leu Pro Gly Val Ser Leu Ala Trp Gly
 3700 3705 3710

Leu Trp Glu Glu Ala Ser Gly Met Thr Gly His Leu Ala Gly Thr Asp
 3715 3720 3725

His Arg Arg Ile Ile Arg Ser Gly Leu His Pro Met Ser Thr Pro Asp
 3730 3735 3740

Ala Leu Ala Leu Phe Asp Ala Ala Leu Ala Leu Asp Arg Pro Val Leu
 3745 3750 3755 3760

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Leu Pro Ala Asp Leu Arg Pro Ala Pro Pro Leu Pro Pro Leu Leu Gln
3765 3770 3775

Asp Leu Leu Pro Ala Thr Arg Arg Arg Thr Thr Arg Thr Thr Thr Thr
3780 3785 3790

Gly Gly Ala Asp Asn Gly Ala Gln Leu His Ala Arg Leu Ala Gly Gln
3795 3800 3805

Thr His Glu Gln Gln His Thr Thr Leu Leu Ala Leu Val Arg Ser His
3810 3815 3820

Ile Ala Thr Val Leu Gly His Thr Thr Pro Asp Thr Ile Pro Pro Asp
3825 3830 3835 3840

Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu
3845 3850 3855

Arg Asn Arg Leu Ser Arg Thr Thr Gly Leu Arg Leu Pro Thr Thr Leu
3860 3865 3870

Ala Phe Asp His Pro Asn Pro Thr Thr Leu Thr His His Leu His Thr
3875 3880 3885

Gln Leu Gln Pro Gln Pro Asp Asn Ala Val Ala Pro Val Leu Ala Glu
3890 3895 3900

Leu Asp Lys Leu Glu Ser Ala Leu Ser Ala Leu Asp Lys Thr Asp Ser
3905 3910 3915 3920

Ala Ser Glu Arg Val Thr Leu Arg Leu Lys Ser Leu Met Leu Arg Trp
3925 3930 3935

Asn Ala Pro Gln His Pro Thr Ala Glu Ser Ala Asp Asp Asp Glu Lys
3940 3945 3950

Phe Thr Ser Ala Thr Glu Ala Glu Ile Phe Lys Phe Ile Asp Asn Asp

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3955

3960

3965

Leu Gly Leu Ser

3970

<210> 4

<211> 6239

<212> PRT

<213> Streptomyces avermitilis

<400> 4

Met Gln Leu Ala Asn Glu Ala Lys Leu Leu Glu Tyr Leu Lys Arg Val

1

5

10

15

Thr Ala Asp Leu Asp Arg Thr Arg Arg Arg Leu Tyr Glu Val Val Glu

20

25

30

Arg Glu Gln Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Tyr Pro

35

40

45

Gly Gly Ala Thr Ser Pro Thr Arg Leu Trp His Leu Val Lys Ser Gln

50

55

60

Thr Asp Ala Ile Gly Glu Phe Pro Thr Asp Arg Gly Trp Asn Leu Glu

65

70

75

80

Gln Leu Tyr Asp Pro Asp Pro Asp Arg Ser Gly Thr Ser Tyr Thr Arg

85

90

95

Ser Gly Gly Phe Leu Tyr Asp Ala Gly Asp Phe Asp Ala Ala Phe Phe

100

105

110

Glu Leu Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu

115

120

125

Leu Leu Glu Thr Thr Trp Glu Thr Phe Glu Gln Gly Gly Ile Asp Pro

130

135

140

158/245

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Arg Ser Met Arg Gly Ser Arg Thr Gly Val Phe Val Gly Ile Asn Pro
145 150 155 160

Glu Asp Tyr Thr Thr Gly Tyr Thr His Gln Pro Ser Asn Ala Val Glu
165 170 175

Gly Tyr Leu Leu Thr Gly Ser Ala Ala Ser Ile Ala Ser Gly Arg Ile
180 185 190

Ser Tyr Asn Phe Gly Leu Glu Gly Pro Ala Ile Thr Ile Asp Thr Ala
195 200 205

Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala Leu Arg
210 215 220

Ser Gly Glu Cys Thr Met Ala Leu Ala Gly Gly Ala Ser Val Met Ala
225 230 235 240

Thr Pro Phe Val Phe Thr Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala
245 250 255

Asp Gly Arg Cys Lys Ala Phe Ser Ala Ala Ala Asp Gly Thr Gly Trp
260 265 270

Ser Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Arg
275 280 285

Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn
290 295 300

Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Arg Ser Gln
305 310 315 320

Val Lys Val Ile Arg Gln Ala Leu Ala Asn Ala His Leu Ser Pro Ala
325 330 335

Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Thr Leu Gly Asp

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340

345

350

Pro Ile Glu Ala Gln Ala Leu Val Glu Ala Tyr Gly Gln Asp Arg Pro
355 360 365

Asn Gly Arg Pro Leu Trp Leu Gly Thr Leu Lys Ser Asn Ile Gly His
370 375 380

Ser Met Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala
385 390 395 400

Leu Arg Asn Gly Leu Leu Pro Arg Thr Leu His Val Asp Glu Pro Ser
405 410 415

Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu Leu Thr Glu Thr
420 425 430

Val Pro Trp Pro Gly Gly Glu Gly Arg Leu Arg Arg Ala Gly Val Ser
435 440 445

Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu Ala
450 455 460

Pro Ala His Asn Ile Pro Ser Asp Thr Pro Ala Asp Asp Val Pro Gly
465 470 475 480

Glu Ser Ala Ala Asp Glu Asp Ala Gly Ser Gly Asp Glu Ala Ala Ala
485 490 495

Gly Ser Pro Gly Val Trp Pro Trp Leu Val Ser Ala Lys Ser Gln Pro
500 505 510

Ala Leu Arg Ala Gln Ala Gln Ala Leu His Ala His Leu Thr Asp His
515 520 525

Pro Gly Leu Asp Leu Ala Asp Val Gly Tyr Thr Leu Ala His Ala Arg
530 535 540

Ala Val Phe Asp His Arg Ala Thr Leu Ile Ala Ala Asp Arg Asp Thr
545 550 555 560

Phe Leu Gln Ala Leu Gln Ala Leu Ala Ala Gly Glu Pro His Pro Ala
565 570 575

Val Ile His Ser Ser Ala Pro Gly Gly Thr Gly Thr Gly Glu Ala Ala
580 585 590

Gly Lys Thr Ala Phe Ile Cys Ser Gly Gln Gly Thr Gln Arg Pro Gly
595 600 605

Met Ala His Gly Leu Tyr His Thr His Pro Val Phe Ala Ala Ala Leu
610 615 620

Asn Asp Ile Cys Thr His Leu Asp Pro His Leu Asp His Pro Leu Leu
625 630 635 640

Pro Leu Leu Thr Gln Asp Pro Asn Thr Gln Asp Thr Thr Thr Leu Glu
645 650 655

Glu Ala Ala Ala Leu Leu Gln Gln Thr Arg Tyr Ala Gln Pro Ala Leu
660 665 670

Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr Asp Gly Tyr His
675 680 685

Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly Glu Ile Thr Ala
690 695 700

Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala Thr Thr Leu Ile
705 710 715 720

Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro Gly Thr Met Thr
725 730 735

Thr Leu His Thr Thr Pro His His Ile Thr His His Leu Thr Ala His
740 745 750

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Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro Thr Ser Leu Val
755 760 765

Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr Thr Leu Cys Gln
770 775 780

Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Asn His Ala Phe His
785 790 795 800

Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His Gln His Thr Gln
805 810 815

Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile Thr Ala Asn Thr
820 825 830

Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr Gln Gln Ala Arg
835 840 845

Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr Leu His Gln His Gly
850 855 860

Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr Leu Thr Thr Leu
865 870 875 880

Thr His Asp Asn Leu Pro Asn Thr Pro Thr Thr Thr Leu Thr Leu Thr
885 890 895

His Pro His His His Pro Gln Thr His Leu Leu Thr Asn Leu Ala Lys
900 905 910

Thr Thr Thr Thr Trp His Pro His His Tyr Thr His His His Asn Gln
915 920 925

Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr Pro Phe Gln His
930 935 940

His His Tyr Trp Leu Gln Pro Pro Gly Lys Pro Ser Asp Pro Ser Pro

945 950 955 960

Ser Glu Gly Arg Glu Gln Ala Thr Thr Pro Ser Thr Pro Leu Arg Asp
965 970 975

Val Leu Val Gly Lys Ser Pro Gln Glu Arg Asp Glu Glu Leu Leu Arg
980 985 990

Leu Val Arg Thr His Ala Ala Ala Val Leu Gly His Ala Thr Pro Glu
995 1000 1005

Val Ile Val Pro Asn Lys Ala Phe Lys Glu Leu Gly Phe Asp Ser Leu
1010 1015 1020

Ala Ala Ile Gln Leu Arg Asn Arg Leu Leu Ala Asp Val Asp Leu Pro
1025 1030 1035 1040

Leu Pro Ala Thr Leu Ile Phe Asp Tyr Pro Thr Pro Met Ala Leu Cys
1045 1050 1055

Gln Phe Leu Arg Ala Ala Ile Val Gly Ala Asp Thr Gly Thr Thr Thr
1060 1065 1070

Arg Leu Pro Leu Thr Ala Val Pro Ala Asp Glu Pro Ile Ala Ile Val
1075 1080 1085

Gly Met Ala Cys Arg Tyr Pro Gly Asp Val Arg Thr Val Asp Asp Leu
1090 1095 1100

Trp Gln Val Val Ser Gly Gly His Asp Ala Ile Gly Gly Phe Pro Thr
1105 1110 1115 1120

Asn Arg Gly Trp Asp Leu Asp Thr Leu Tyr Asn Pro Asp Pro Asp His
1125 1130 1135

His Gly Thr Ser Tyr Thr Arg Ser Gly Gly Phe Leu Tyr Asp Ala Gly
1140 1145 1150

Asn Phe Asp Pro Asp Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala
 1155 1160 1165

Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Thr Ala Trp Glu Ser Ile
 1170 1175 1180

Glu His Ala Cys Ile Asn Pro Asp Ser Leu Arg Gly Thr Pro Thr Gly
 1185 1190 1195 1200

Val Phe Ala Gly Leu Thr Tyr His Asp Tyr Ala Ala Arg Phe Pro Thr
 1205 1210 1215

Ala Pro Ala Gly Phe Glu Gly Tyr Leu Gly His Gly Ser Ala Gly Ser
 1220 1225 1230

Ile Ala Ser Gly Arg Val Ala Tyr Ala Leu Gly Leu Glu Gly Pro Ala
 1235 1240 1245

Leu Thr Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu
 1250 1255 1260

Ala Cys Gln Ala Leu Arg Ser Gly Glu Cys Ser Met Ala Leu Ala Gly
 1265 1270 1275 1280

Gly Val Thr Val Met Ser Thr Pro Ala Gly Phe Val Glu Phe Ser Arg
 1285 1290 1295

Gln Arg Gly Leu Ala Val Asp Gly Arg Cys Lys Ala Phe Ser Ala Ala
 1300 1305 1310

Ala Asp Gly Thr Gly Trp Gly Glu Gly Val Gly Met Leu Leu Val Glu
 1315 1320 1325

Arg Leu Ser Asp Ala Arg Arg Leu Gly His Arg Ile Leu Ala Val Val
 1330 1335 1340

Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala
 1345 1350 1355 1360

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Pro Asn Gly Pro Ser Gln Glu Arg Val Ile Arg Leu Ala Leu Ala Asn
 1365 1370 1375

Ala Asp Leu Thr Pro Ala Asp Val Asp Ala Val Glu Ala His Gly Thr
 1380 1385 1390

Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr
 1395 1400 1405

Tyr Gly Gln Asp Arg Pro Gly Asn Glu Pro Leu Trp Leu Gly Ser Met
 1410 1415 1420

Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala Gly Val Gly Gly Val
 1425 1430 1435 1440

Ile Lys Met Val Met Ala Leu Arg Asn Gly Leu Leu Pro Arg Thr Leu
 1445 1450 1455

His Val Asp Glu Pro Ser Pro His Val Asp Trp Ser Ala Gly Ala Val
 1460 1465 1470

Gln Leu Leu Thr Glu Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Leu
 1475 1480 1485

Arg Arg Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His
 1490 1495 1500

Val Ile Leu Glu Glu Ala Pro Ala His Asn Ile Pro Ser Asp Thr Pro
 1505 1510 1515 1520

Ala Asp Asp Ala Pro Gly Glu Ala Ala Ala Asp Asp Val Pro Gly Glu
 1525 1530 1535

Ala Ala Gly Asp Asp Ala Gly Thr Gly Gly Glu Ala Thr Gly Pro Ala
 1540 1545 1550

Ala Gly Ser Pro Gly Val Trp Pro Trp Leu Val Ser Ala Lys Ser Gln

1555

1560

1565

Pro Ala Leu Arg Ala Gln Ala Gln Ala Leu His Ala His Leu Thr Asp

1570

1575

1580

His Pro Gly Leu Asp Leu Ala Asp Val Gly Tyr Thr Leu Ala His Ala

1585

1590

1595

1600

Arg Ala Val Phe Asp His Arg Ala Thr Leu Ile Ala Ala Asp Arg Asp

1605

1610

1615

Thr Phe Leu Gln Ala Leu Gln Ala Leu Ala Ala Gly Glu Pro His Pro

1620

1625

1630

Ala Val Ile His Ser Ser Ala Pro Gly Gly Thr Gly Thr Gly Glu Ala

1635

1640

1645

Ala Gly Lys Thr Ala Phe Ile Cys Ser Gly Gln Gly Thr Gln Arg Pro

1650

1655

1660

Gly Met Ala His Gly Leu Tyr His Thr His Pro Val Phe Ala Ala Ala

1665

1670

1675

1680

Leu Asn Asp Ile Cys Thr His Leu Asp Pro His Leu Asp His Pro Leu

1685

1690

1695

Leu Pro Leu Leu Thr Gln Asp Pro Asn Thr Gln Asp Thr Thr Thr Leu

1700

1705

1710

Glu Glu Ala Ala Ala Leu Leu Gln Gln Thr Pro Tyr Ala Gln Pro Ala

1715

1720

1725

Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr Asp Gly Tyr

1730

1735

1740

His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly Glu Ile Thr

1745

1750

1755

1760

Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala Thr Thr Leu
 1765 1770 1775

Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro Gly Thr Met
 1780 1785 1790

Thr Thr Leu His Thr Thr Pro His His Ile Thr His His Leu Thr Ala
 1795 1800 1805

His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro Thr Ser Leu
 1810 1815 1820

Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr Thr Leu Cys
 1825 1830 1835 1840

Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Lys Asn Ala Phe
 1845 1850 1855

His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His Gln His Thr
 1860 1865 1870

Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile Thr Ala Asn
 1875 1880 1885

Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr Gln Gln Ala
 1890 1895 1900

Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr Leu His Gln His
 1905 1910 1915 1920

Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr Leu Thr Thr
 1925 1930 1935

Leu Thr His His Asn Leu Pro Asn Thr Pro Thr Thr Thr Leu Thr Leu
 1940 1945 1950

Thr His Pro His His His Pro Gln Thr His Leu Leu Thr Asn Leu Ala
 1955 1960 1965

Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr His His His Asn
1970 1975 1980

Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr Pro Phe Gln
1985 1990 1995 2000

His Gln His Tyr Trp Leu Glu Ser Thr Gln Pro Gly Ala Gly Ser Gly
2005 2010 2015

Ser Gly Ser Gly Ser Gly Arg Ala Gly Thr Ala Gly Gly Thr Ala Glu
2020 2025 2030

Val Glu Ser Arg Phe Trp Asp Ala Val Ala Arg Gln Asp Leu Glu Thr
2035 2040 2045

Val Ala Thr Thr Leu Ala Val Pro Pro Ser Ala Gly Leu Asp Thr Val
2050 2055 2060

Val Pro Ala Leu Ser Ala Trp His Arg His Gln His Asp Gln Ala Arg
2065 2070 2075 2080

Ile Asn Thr Trp Thr Tyr Gln Glu Thr Trp Lys Pro Leu Thr Leu Pro
2085 2090 2095

Thr Thr His Gln Pro His Gln Thr Trp Leu Ile Ala Ile Pro Glu Thr
2100 2105 2110

Gln Thr His His Pro His Ile Thr Asn Ile Leu Thr Asn Leu His His
2115 2120 2125

His Gly Ile Thr Pro Ile Pro Leu Thr Leu Asn His Thr His Thr Asn
2130 2135 2140

Pro Gln His Leu His His Thr Arg Gln Gln Ala Gln Asn His Thr Thr
2145 2150 2155 2160

Gly Pro Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu Asp Glu Thr Pro

2165

2170

2175

His Pro His His Pro His Thr Pro Thr Gly Thr Leu Leu Asn Leu Thr
 2180 2185 2190

Leu Thr Gln Thr His Thr Gln Thr His Pro Pro Thr Pro Leu Trp Tyr
 2195 2200 2205

Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp Pro Leu Thr His
 2210 2215 2220

Pro Thr Gln Ala Gln Thr Trp Gly Leu Ala Arg Thr Thr Leu Leu Glu
 2225 2230 2235 2240

His Pro Thr His Thr Ala Gly Ile Ile Asp Leu Pro Thr Thr Pro Thr
 2245 2250 2255

Pro His Thr Leu His His Leu Thr Gln Thr Leu Thr Gln Pro His His
 2260 2265 2270

Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His Thr Arg Arg Leu
 2275 2280 2285

Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro Thr Pro Thr Pro
 2290 2295 2300

His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala Leu Ala Thr His
 2305 2310 2315 2320

Leu Thr His His Leu Thr Thr His Gln Pro Thr Gln His Leu Leu Leu
 2325 2330 2335

Thr Ser Arg Thr Gly Pro His Thr Pro His Ala Gln His Leu Thr Thr
 2340 2345 2350

Gln Leu Gln Gln Lys Gly Ile His Leu Thr Ile Thr Thr Cys Asp Thr
 2355 2360 2365

Ser Asn Pro Asp Gln Leu Gln Gln Leu Leu Asn Thr Ile Pro Pro Gln
 2370 2375 2380

His Pro Leu Thr Thr Val Ile His Thr Ala Gly Ile Leu Asp Asp Ala
 2385 2390 2395 2400

Thr Leu Thr Asn Leu Thr Pro Thr Gln Leu Asn Asn Val Leu Arg Ala
 2405 2410 2415

Lys Ala His Ser Ala His Leu Leu His Gln Leu Thr Gln His Thr Pro
 2420 2425 2430

Leu Asn Ala Phe Val Leu Tyr Ser Ser Ala Ala Ala Thr Phe Gly Ala
 2435 2440 2445

Pro Gly Gln Ala Asn Tyr Ala Ala Ala Asn Ala Tyr Leu Asp Ala Leu
 2450 2455 2460

Ala His His Arg His Thr His His Leu Pro Ala Thr Ser Ile Ala Trp
 2465 2470 2475 2480

Gly Thr Trp Gln Gly Asn Gly Leu Ala Thr Gly Gln Val Ser Glu His
 2485 2490 2495

Leu Arg Arg Arg Gly Met Phe Ala Met Pro Pro Glu Leu Ala Val Thr
 2500 2505 2510

Ala Val Asp Gly Ala Ile Ala Ser Gly Arg Pro Ser Leu Leu Val Ala
 2515 2520 2525

Asp Ile Asp Trp Lys Lys Leu Gly Pro Val Leu Ser Ser Lys Ser Ser
 2530 2535 2540

Val Leu Leu Glu Asp Leu Pro Gln Ala Gln Gly Thr Glu Glu Ala Arg
 2545 2550 2555 2560

Ser Thr Val Glu Gln Thr Glu Ser Thr Asn Leu Arg Gln Leu Leu Met
 2565 2570 2575

094406 094404

Gly Arg Ser Arg Ser Glu Gln Glu Glu Glu Leu Leu Ser Leu Val Arg
2580 2585 2590

Ile His Ser Ala Ala Val Leu Gly Arg Asp Asp Ser Glu Ala Ile Pro
2595 2600 2605

Pro Gly Arg Leu Phe Arg Asp Leu Gly Phe Asp Ser Leu Ala Ala Val
2610 2615 2620

Glu Leu Arg Asn His Leu Ala Ala Gln Thr Glu Leu Ala Leu Pro Thr
2625 2630 2635 2640

Thr Leu Val Phe Asp Tyr Pro Ser Pro Thr Lys Leu Ala Gln Phe Leu
2645 2650 2655

Leu Ser Glu Ile Ala Glu Phe Gln Pro Asp Asn Ser Thr Pro Leu Pro
2660 2665 2670

Arg Pro Arg Ala Glu Leu Asp Glu Pro Ile Ala Ile Val Gly Met Ala
2675 2680 2685

Cys Arg Phe Pro Gly Gly Val Thr Ser Ala Asp Asp Phe Trp Asp Leu
2690 2695 2700

Ile Ser Ser Glu Gln Asp Ala Ile Gly Gly Phe Pro Thr Asp Arg Gly
2705 2710 2715 2720

Trp Asp Leu Asp Thr Leu Tyr Asp Pro Asp Pro Asp His Pro Gly Thr
2725 2730 2735

Cys Tyr Thr Arg Asn Gly Gly Phe Leu Tyr Asp Ala Gly His Phe Asp
2740 2745 2750

Ala Glu Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro
2755 2760 2765

Gln Gln Arg Leu Leu Leu Glu Thr Ala Trp Glu Thr Ile Glu His Ala

2770

2775

2780

Gly Ile Asn Pro His Thr Leu His Gly Thr Pro Thr Gly Val Phe Thr

2785

2790

2795

2800

Gly Thr Asn Gly Gln Asp His Ala Ala His Ile Arg Gln Ala Pro Ser

2805

2810

2815

Gly Thr Glu Gly Phe Val Leu Thr Gly Ala Ala Thr Ser Ile Ala Ser

2820

2825

2830

Gly Arg Ile Ser Tyr Ile Leu Gly Leu Glu Gly Pro Ala Val Thr Leu

2835

2840

2845

Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln

2850

2855

2860

Ser Leu Arg Ser Gly Glu Cys Thr Met Ala Leu Ala Gly Gly Ala Thr

2865

2870

2875

2880

Val Met Thr Thr Pro Ile Thr Phe Thr Glu Phe Ala Arg Gln Arg Gly

2885

2890

2895

Leu Ala Pro Asp Gly Arg Cys Lys Ala Phe Ser Ala Ala Ala Asp Gly

2900

2905

2910

Thr Gly Trp Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser

2915

2920

2925

Asp Ala Arg Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser

2930

2935

2940

Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly

2945

2950

2955

2960

Pro Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Asp Leu

2965

2970

2975

Thr Pro Ala Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Thr
2980 2985 2990

Leu Gly Asp Pro Ile Glu Ala Gln Ala Ile Leu Ala Thr Tyr Gly Gln
2995 3000 3005

Asp Arg Pro Gly Asn Gly Pro Leu Trp Leu Gly Ser Val Lys Ser Asn
3010 3015 3020

Val Gly His Thr Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met
3025 3030 3035 3040

Val Met Ala Leu Arg His Arg Thr Leu Pro Pro Thr Leu His Ala Asp
3045 3050 3055

Glu Pro Ser Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu Leu
3060 3065 3070

Thr Glu Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Pro Arg Arg Ala
3075 3080 3085

Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu
3090 3095 3100

Glu Glu Ala Pro Ala Asp Asp Val Pro Gly Gly Pro Pro Ala Asp Glu
3105 3110 3115 3120

Asp Ala Gly Ser Gly Glu Glu Ala Ala Ala Gly Ser Pro Gly Val Trp
3125 3130 3135

Pro Trp Leu Val Ser Ala Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala
3140 3145 3150

Gln Ala Leu His Ala His Leu Thr Asp His Pro Gly Leu Asp Leu Ala
3155 3160 3165

Asp Val Gly Tyr Thr Leu Ala His Ala Arg Ala Val Phe Asp His Arg
3170 3175 3180

Ala Thr Leu Ile Ala Ala Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln
3185 3190 3195 3200

Ala Leu Ala Ala Gly Glu Pro His Pro Ala Val Ile His Ser Ser Ala
3205 3210 3215

Pro Gly Gly Thr Gly Thr Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile
3220 3225 3230

Cys Ser Gly Gln Gly Thr Gln Arg Pro Gly Met Ala His Gly Leu Tyr
3235 3240 3245

His Thr His Pro Val Phe Ala Ala Ala Leu Asn Asp Ile Cys Thr His
3250 3255 3260

Leu Asp Pro His Leu Asp His Pro Leu Leu Pro Leu Leu Thr Gln Asn
3265 3270 3275 3280

Asp Asn Asp Asn Asp Asn Glu Asp Ala Ala Ala Leu Leu Gln Gln Thr
3285 3290 3295

Pro Tyr Ala Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg
3300 3305 3310

Leu Leu Thr Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His
3315 3320 3325

Ser Leu Gly Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu
3330 3335 3340

Thr Asp Ala Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr
3345 3350 3355 3360

Met Pro Pro Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile
3365 3370 3375

Thr His His Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile

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3380

3385

3390

Asn Thr Pro Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln

3395

3400

3405

His Ile Thr Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu

3410

3415

3420

Pro Thr Asn His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn

3425

3430

3435

3440

Gln Leu His Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr

3445

3450

3455

Pro Leu Ile Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His

3460

3465

3470

Tyr Trp Thr Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr

3475

3480

3485

Gln Thr Leu His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro

3490

3495

3500

Asp Asn Thr Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Thr Pro

3505

3510

3515

3520

Thr Thr Thr Leu Thr Leu Thr His Pro His His His Pro Gln Thr His

3525

3530

3535

Leu Leu Thr Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His

3540

3545

3550

Tyr Thr His His His Asn Gln Pro His Thr His Thr His Leu Asp Leu

3555

3560

3565

Pro Thr Tyr Pro Phe Gln His His His Tyr Trp Leu Glu Leu Pro Ser

3570

3575

3580

Ala Gln Thr Ser Pro Gly Gln Arg Arg Ser Arg Arg Ser Ala Pro Asp
 3585 3590 3595 3600

Thr Ala Glu Ser Glu Phe Trp Asp Ala Val Asn Glu Glu Asp Leu Gln
 3605 3610 3615

Ser Leu Ala Glu Thr Leu Asp Ile Asp Ala Ser Ala Leu Asp Thr Val
 3620 3625 3630

Val Pro Ala Leu Ser Ala Trp His Arg His Gln His Asp Gln Ala Arg
 3635 3640 3645

Ile Asn Thr Trp Thr Tyr Gln Glu Thr Trp Lys Pro Leu Thr Leu Pro
 3650 3655 3660

Thr Thr His Gln Pro His Gln Thr Trp Leu Ile Ala Ile Pro Glu Thr
 3665 3670 3675 3680

Gln Thr His His Pro His Ile Thr Asn Ile Leu Thr Asn Leu His His
 3685 3690 3695

His Gly Ile Thr Pro Ile Pro Leu Thr Val Asn His Thr His Thr Asn
 3700 3705 3710

Pro Gln His Leu His His Thr Leu His His Thr Arg Gln Gln Ala Gln
 3715 3720 3725

Asn His Thr Thr Gly Pro Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu
 3730 3735 3740

Asp Glu Thr Pro His Pro His His Pro His Thr Pro Thr Gly Thr Leu
 3745 3750 3755 3760

Leu Asn Leu Thr Leu Pro Gln Thr His Thr Gln Thr His Pro Pro Thr
 3765 3770 3775

Pro Leu Trp Tyr Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp
 3780 3785 3790

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T04230 9824T660

Pro Leu Thr His Pro Thr Gln Ala Gln Thr Trp Gly Leu Ala Arg Thr
3795 3800 3805

Thr Leu Leu Glu His Pro Thr His Thr Ala Gly Ile Ile Asp Leu Pro
3810 3815 3820

Thr Thr Pro Thr Pro His Thr Leu His His Leu Thr Gln Thr Leu Thr
3825 3830 3835 3840

Gln Pro His His Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His
3845 3850 3855

Thr Arg Arg Leu Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro
3860 3865 3870

Thr Pro Thr Pro His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala
3875 3880 3885

Leu Ala Thr His Leu Thr His His Leu Thr Thr His Gln Pro Thr Gln
3890 3895 3900

His Leu Leu Leu Thr Ser Arg Thr Gly Pro His Thr Pro His Ala Gln
3905 3910 3915 3920

His Leu Thr Thr Gln Leu Gln Gln Lys Gly Ile His Leu Thr Ile Thr
3925 3930 3935

Thr Cys Asp Thr Ser Asn Pro Asp Gln Leu Gln Gln Leu Leu Asn Thr
3940 3945 3950

Ile Pro Pro Gln His Pro Leu Thr Thr Val Ile His Thr Ala Gly Val
3955 3960 3965

Asn Leu Phe Ala Pro Val Ser Glu Thr Asp Ala Glu Ser Phe Ser Ser
3970 3975 3980

Val Thr Ala Ala Lys Ala Thr Gly Ala Ala Ile Leu His Glu Leu Leu

3985

3990

3995

4000

Leu Asp His Glu Thr Leu Glu His Phe Ile Leu Phe Ser Ser Gly Ala
 4005 4010 4015

Gly Ala Trp Gly Ser Gly Asn Gln Cys Ala Tyr Ser Ala Ala Asn Ala
 4020 4025 4030

Tyr Leu Asp Ala Leu Ala Thr His Arg Gln Thr His Gly Leu Pro Gly
 4035 4040 4045

Ala Ser Ile Ala Trp Gly Pro Trp Ala Gly Lys Gly Met Ser Ala Gly
 4050 4055 4060

Asp Ala Ala His Gly Tyr Leu Glu Lys Arg Gly Ile Leu Pro Met Glu
 4065 4070 4075 4080

Pro Arg Met Ala Leu Ala Ala Phe His Arg Ala Arg Ala Gln Arg Pro
 4085 4090 4095

Asn Ser Asn Leu Ile Ile Ala Asp Ile Asp Trp Glu Arg Phe Val Pro
 4100 4105 4110

Ala Phe Thr Ala Arg Arg His Ser Pro Leu Ile Glu Asp Ile Pro Glu
 4115 4120 4125

Val Arg Gln Ala Ala Gln Glu Leu Glu Ala Ala Ala Ser Thr Ala Lys
 4130 4135 4140

Thr Thr Thr Ala Gln Pro Ile Ala Thr Ser Leu Arg Glu Arg Leu Ala
 4145 4150 4155 4160

Arg Leu Thr Ser Ser Lys Gln Asn Gln Val Leu Leu Gly Leu Ile Arg
 4165 4170 4175

Thr Gly Ile Cys Thr Val Leu Gly Leu Arg Asn Pro Glu Gly Ile Glu
 4180 4185 4190

Asp Gln Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ser Ala
4195 4200 4205

Gln Phe Ser Lys Glu Leu Ala Lys Glu Thr Gly Leu Pro Leu Pro Pro
4210 4215 4220

Ser Leu Val Phe Asp Tyr Pro Thr Pro Gln Glu Cys Ala Ala His Leu
4225 4230 4235 4240

Arg Thr Gln Leu Val Asp Leu Asp Asp Glu Glu Asp Ala Ala Leu Ser
4245 4250 4255

Asn Ala Leu Pro Gln Val Ala His Arg Arg Thr Val Glu Asp Glu Pro
4260 4265 4270

Ile Ala Ile Ile Gly Met Ala Cys Arg Phe Pro Gly Gly Val Arg Ser
4275 4280 4285

Ala Asp Asp Leu Trp Glu Leu Leu Ala Ser Gly Lys Asp Ala Ile Gly
4290 4295 4300

Val Phe Pro Thr Asp Arg Gly Trp Asp Leu Asp Thr Leu Tyr Asp Pro
4305 4310 4315 4320

Asp Pro Asp His Pro Gly Thr Cys Tyr Thr Arg Asn Gly Gly Phe Leu
4325 4330 4335

Tyr Gly Ala Gly His Phe Asp Ala Glu Phe Phe Gly Ile Ser Pro Arg
4340 4345 4350

Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Thr Ala
4355 4360 4365

Trp Glu Thr Ile Glu His Ala Gly Ile Asn Pro His Thr Leu His Gly
4370 4375 4380

Thr Pro Thr Gly Val Phe Ala Gly Ile Asn Ala Gln Asp His Ala Ala
4385 4390 4395 4400

4595

4600

4605

Leu Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Ala Gln Ala Ala
 4610 4615 4620

Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala Leu Arg Asn Gly
 4625 4630 4635 4640

Leu Leu Pro Gln Thr Leu His Val Asp Glu Pro Thr Pro Gln Val Asp
 4645 4650 4655

Trp Ser Thr Gly Ala Val Gln Leu Leu Thr Gln Pro Val Pro Trp Pro
 4660 4665 4670

Ala Asp Pro Ala Gly Arg Pro Arg His Ala Gly Val Ser Ser Phe Gly
 4675 4680 4685

Val Ser Gly Thr Asn Ala His Ile Ile Leu Glu Glu Ala Pro Thr Pro
 4690 4695 4700

Gln Asp Ser Asp Thr Asp Asp Glu Pro Pro Ala Asn Ala Pro Ala Leu
 4705 4710 4715 4720

Pro His Pro Leu Pro Leu Pro Val Pro Val Ser Ala Arg Ser Glu Ala
 4725 4730 4735

Gly Leu Arg Ala Gln Ala Gln Ala Leu Arg Gln Tyr Val Ala Ala Arg
 4740 4745 4750

Pro Asp Met Ser Pro Ala Asp Ile Gly Ala Gly Leu Ala Arg Gly Arg
 4755 4760 4765

Ala Val Leu Glu His Arg Ala Val Ile Leu Ala Ala Asp Arg Glu Glu
 4770 4775 4780

Leu Ala Gln Ala Leu Thr Ala Leu Ala Ala Gly Glu Pro His Pro His
 4785 4790 4795 4800

Ile Thr Thr Gly His Thr Arg Gly Gly Asp Arg Gly Gly Val Val Phe
 4805 4810 4815

Val Phe Pro Gly Gln Gly Gly Gln Trp Ala Gly Met Gly Leu Thr Leu
 4820 4825 4830

Leu Thr Ser Ser Pro Val Phe Ala Glu His Ile Asp Ala Cys Glu Lys
 4835 4840 4845

Ala Leu Thr Pro Trp Val Pro Trp Ser Leu Thr Asp Ile Leu His Arg
 4850 4855 4860

Asp Pro Asp Asp Pro Ala Trp Gln Gln Ala Asp Val Val Gln Pro Val
 4865 4870 4875 4880

Leu Phe Ser Ile Met Val Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly
 4885 4890 4895

Ile Glu Pro Asp Ala Val Leu Gly His Ser Gln Gly Glu Ile Ala Ala
 4900 4905 4910

Ala His Ile Cys Gly Ala Leu Ser Leu Lys Asp Ala Ala Lys Thr Val
 4915 4920 4925

Ala Leu Arg Ser Arg Ala Leu Ala Ala Val Arg Gly Arg Gly Ala Met
 4930 4935 4940

Ala Ser Leu Pro Leu Pro Ala Gln Asp Val Gln Gln Leu Ile Ser Glu
 4945 4950 4955 4960

Arg Trp Glu Gly Gln Leu Trp Val Ala Ala Leu Asn Gly Pro His Ser
 4965 4970 4975

Thr Thr Val Ser Gly Asp Thr Lys Ala Val Asp Glu Val Leu Ala His
 4980 4985 4990

Cys Thr Asp Thr Gly Leu Arg Ala Lys Arg Ile Pro Val Asp Tyr Ala
 4995 5000 5005

Ser His Cys Pro His Val Gln Pro Leu His Asp Glu Leu Leu His Leu
 5010 5015 5020

Leu Gly Asp Ile Thr Pro Gln Pro Ser Thr Val Pro Phe Phe Ser Thr
 5025 5030 5035 5040

Val Glu Gly Thr Trp Leu Asp Thr Thr Thr Leu Asp Ala Ala Tyr Trp
 5045 5050 5055

Tyr Arg Asn Leu His Gln Pro Val Arg Phe Ser His Ala Ile Gln Thr
 5060 5065 5070

Leu Thr Asp Asp Gly His Arg Ala Phe Ile Glu Ile Ser Pro His Pro
 5075 5080 5085

Thr Leu Val Pro Ala Ile Glu Asp Thr Thr Glu Asn Thr Thr Glu Asn
 5090 5095 5100

Ile Thr Ala Thr Gly Ser Leu Arg Arg Gly Asp Asn Asp Thr His Arg
 5105 5110 5115 5120

Phe Leu Thr Ala Leu Ala His Thr His Thr Thr Gly Ile Gly Thr Pro
 5125 5130 5135

Thr Thr Trp His His His Tyr Thr Gln Thr His Pro His Pro Asn Pro
 5140 5145 5150

His Thr His Leu Asp Leu Pro Thr Tyr Pro Phe Gln His Gln His Tyr
 5155 5160 5165

Trp Leu Gln Pro Pro Thr Thr Thr Thr Asp Leu Thr Thr Thr Gly Leu
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Thr Pro Thr His His Pro Leu Leu Thr Ala Thr Leu Thr Leu Ala Asp
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Asn Asn Thr Gln Leu Leu Thr Gly Arg Leu Ser Leu Arg Thr His Pro

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Trp Leu Thr Asp His Thr Val Ala Gly Met Val Leu Leu Pro Gly Thr
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Ala Leu Leu Glu Leu Ala Leu Gln Ala Gly Glu Arg Val Asp Cys Pro
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Arg Val Glu Glu Leu Thr Leu His Ala Pro Leu Val Ile Pro His Thr
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Glu Asp Val Thr Leu Gln Val Thr Val Arg Ala Ala Asp Glu Ser Gly
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His Arg Ala Leu Ala Ile His Ser Tyr Ser Gly Thr Ala Ser Ser Ala
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Asp Arg Glu Trp Thr Arg His Ala Thr Gly Leu Leu Thr His His Ala
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Asp Thr Asp His Arg Ala Asp Thr His Thr Asp Ala Cys Leu Gly Gly
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Ser Trp Pro Pro Pro Gly Ala Gln Pro Ile Glu Leu Gly Asp Val Tyr
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Gly Arg Met Ala Ala Asp Ser Asp Ile Ala Tyr Gly Pro Val Phe Gln
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Gly Leu His Ala Ala Trp Arg Phe Gly Asp Asp Val Leu Ala Glu Val
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Arg Leu Pro Glu Glu Ala Leu Arg Asp Ala Pro Ala Ala Ala Phe Gly
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Val His Pro Ala Leu Leu Asp Ala Ala Leu His Ala Thr Ala Leu Thr
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Pro Gln Asn Gly Asp Gly Ser Thr Glu Asn Val Ala Gln Glu Ser Met
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Pro Asp Arg Ala Ala His Gln Ala Arg Leu Pro Phe Ser Trp Ser Gly
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Val Ser Leu His Thr Ala Gly Ser Ser Val Leu Arg Val Arg Leu Ser
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Arg Ser Pro Gln His Gly Asn Ala Val Ala Leu Thr Ala Ala Asp Glu
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Asp Gly Arg Pro Val Val Thr Ile Glu Ser Leu Ala Leu Arg Pro Val
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Ser Thr Glu Glu Leu Arg Ala Ala Ala Asp Arg Thr Pro Glu His Glu
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Ser Leu Phe Arg Leu Asp Trp Val Ser Val Pro Val Pro Ala Asn Ala
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Pro Ser Pro Thr Ala Asp Arg Pro Trp Ala Val Ile Gly Ala Gly Leu
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Pro His Leu Pro Gly Leu Thr Glu His Glu His Val Thr Ala Tyr Asp
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Glu Pro Ala Asp Leu Leu Leu Ala Leu Asp Arg Gly Ala Pro Pro Pro
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Gly Val Leu Val Val Gly Gly Val Ala His Thr Glu Ala Arg Glu Tyr
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Ser Ala Glu Ala Pro Gly Glu Arg Gly Thr Glu Ala Cys Glu Ala Arg
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Pro Asp Val Val His Val Gly Val Val His Thr Ala Ala Val His Ala
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Ala Ala Ala Gln Met Leu Ala Arg Leu Gln Ala Trp Leu Gly Asp Glu
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Phe Thr Pro Arg Leu Val Arg Ala Pro Arg Val Ala Asp Ala Val Pro
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Ala Val Pro Ala Val Ala Val Pro Ser Ala Gly His Ala Ala Val Pro
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Thr Gly Val Leu Gly Arg Leu Val Ala Arg His Leu Val Glu Ala His
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Gly Val Arg His Leu Leu Leu Ala Gly Arg Arg Gly Pro Asp Ala Glu
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Glu Val Val Ala Cys Asp Ala Ala Asp Arg Gln Gln Leu Ala Asp Leu

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5855

Leu Gly Ala Val Leu Arg Ala Lys Ala Asp Ala Ala Leu Leu Leu Asp

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5870

Glu Leu Thr Arg Gly Ala Glu Leu Ser Ala Phe Val Met Phe Ser Ser

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5880

5885

Ala Ser Ala Val Val Gly Ser Pro Gly Gln Gly Asn Tyr Ala Ala Ala

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5895

5900

Asn Ala Val Leu Asp Phe Leu Ala His Arg Arg Arg Ala Glu Gly Leu

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5910

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5920

Pro Ala Val Ser Leu Ala Trp Gly Leu Trp Glu Glu Gly Thr Gly Met

5925

5930

5935

Thr Gly His Leu Asp Val Asp Asp His Ala Arg Ile Ser Arg Ala Gly

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5945

5950

Met Arg Pro Leu Pro Thr Ala Glu Ala Leu Ala Leu Phe Asp Ala Ala

5955

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Leu Ala Asp Gly Glu Pro Phe Leu Met Pro Ala Arg Leu Asp Leu Thr

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Ala Val Arg Ser Gly Ala Ala Ser Ala Pro Val Pro Pro Leu Leu Gln

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5995

6000

Gly Leu Leu Gln Leu Pro Arg Ser Arg Ser Ala Ala Ala Ala Pro Gly

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6010

6015

09914236-002494

His Gly Ala Pro Ala Ala Asp Glu Ala Ala Ala Trp Arg Glu Arg Leu
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Arg Ser His Val Ala Ala Val Leu Gly His Ser Gly Ala Asp Gly Ile
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Asp Ala Ser Arg Ala Phe Arg Glu Leu Gly Phe Asp Ser Leu Thr Ala
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Val Glu Leu Arg Asn Arg Leu Thr Ala Ala Thr Gly Leu Arg Leu Arg
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Ala Thr Leu Ala Phe Asp Phe Pro Thr Pro Ala Ala Leu Ala Glu His
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Leu Gly Glu Arg Leu Leu Pro Asp Gln Glu Ala Thr Gly Glu Gln Ala
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Gly Asp Gln Leu Ser Gly Gly Ser Glu Glu Asp Val Arg Ser Leu Leu
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Thr Ser Ile Pro Ile Gly Arg Leu Arg Asp Ala Gly Leu Leu Gly Pro
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Leu Leu Thr Leu Ala Asp Thr Gly Arg Gly Ala Ser Gly Ala Ala Ala
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Gly Pro Glu Asp Ala Pro Pro Ser Gly Gln Asp Thr Pro Ala Pro Val
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Ser Ile Asp Glu Met Asp Ile Asp Asp Leu Met Asp Leu Ala His Gly
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Ser Ser Arg Asn Arg Thr His His Thr His Glu Gly Glu Thr Ala
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<211> 4881

<212> PRT

<213> Streptomyces avermitilis

<400> 5

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Gln Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Phe Pro Gly Gly
 35 40 45

Val Glu Ser Ala Glu Asp Phe Trp Glu Leu Ile Ala Ser Gly Arg Asp
 50 55 60

Ala Val Gly Glu Phe Pro Val Asp Arg Gly Trp Asp Val Glu Ala Phe
 65 70 75 80

Tyr Asp Pro Glu Pro Gly Arg Ala Gly Ser Ser Tyr Thr Arg Arg Gly
 85 90 95

Gly Phe Leu Glu Gly Ala Ala Glu Phe Asp Ala Gly Phe Phe Gly Ile
 100 105 110

Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Met Leu
 115 120 125

Glu Val Ser Trp Glu Ala Leu Glu Arg Ala Gly Ile Asp Pro Ala Thr
 130 135 140

Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Arg Ala Gly Asp Thr Pro
355 360 365

Val Trp Leu Gly Ser Val Lys Ser Asn Ile Gly His Ala Gln Ala Ala
370 375 380

Ala Gly Val Ala Gly Val Ile Lys Met Val Met Ala Leu Arg Ala Gly
385 390 395 400

Val Leu Pro Arg Thr Leu His Val Asp Glu Pro Ser Ser Gln Val Asp
405 410 415

Trp Ser Ser Gly Ser Val Arg Val Leu Ala Asp Glu Val Glu Trp Pro
420 425 430

Gly Val Glu Gly Arg Leu Arg Arg Ala Gly Val Ser Ala Phe Gly Val
435 440 445

Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu Ala Ser Gly Gly Ala
450 455 460

Gly Gly Gly Ala Gly Arg Leu Gln Glu Leu Gly Pro Gly Val Val Ser
465 470 475 480

Gly Ser Gly Val Val Pro Trp Val Val Ser Ala Arg Ser Glu Leu Ala
485 490 495

Leu Arg Gly Gln Ala Arg Arg Leu Arg Gly Val Val Ala Val Gly Gly
500 505 510

Gly Ala Asp Gly Val Gly Val Ser Pro Ala Gly Val Gly Arg Ala Leu
515 520 525

Val Ser Glu Arg Ser Val Phe Glu His Arg Ala Val Val Val Ala Glu
530 535 540

Asp Arg Asp Glu Phe Leu His Ala Leu Asp Ala Leu Ala Gly Gly Arg

545 550 555 560

Pro Val Pro Gly Val Val Glu Gly Arg Thr Thr Ser Gly Glu Leu Ala
565 570 575

Val Leu Phe Ala Gly Gln Gly Thr Gln Arg Ala Gly Met Gly Arg Glu
580 585 590

Leu Tyr Glu Ala Tyr Pro Val Phe Ala Gln Ala Ile Asp Glu Ile Cys
595 600 605

Ala Glu Ala Asp Thr Ala Arg Thr Asp Pro Gly Ala Pro Gly Leu Arg
610 615 620

Asp Val Leu Phe Ala Pro Gln Asp Ser Pro Glu Gly Arg Leu Ile Glu
625 630 635 640

Asp Thr Gly Phe Ala Gln Pro Ala Leu Phe Ala Phe Glu Val Ala Leu
645 650 655

Phe Arg Leu Leu Glu Thr Trp Gly Leu Thr Pro Asp Tyr Val Leu Gly
660 665 670

His Ser Val Gly Glu Leu Ala Ala Ala His Val Ala Gly Met Leu Cys
675 680 685

Leu Ala Asp Ala Val Ala Leu Val Val Ala Arg Gly Arg Leu Met Gln
690 695 700

Gly Leu Pro Ser Gly Gly Ala Met Val Ala Ile Glu Ala Ser Glu Asp
705 710 715 720

Glu Ile Leu Pro Leu Pro Asp Glu Tyr Ala Ser Arg Val Ala His Ala
725 730 735

Ala Val Asn Gly Pro Arg Ser Ile Val Leu Ser Gly Asp Glu Asp Ala
740 745 750

Val Leu Asp Leu Ala Gln Gln Trp Ala Ala Arg Gly Arg Arg Thr Arg
755 760 765

Arg Leu Arg Thr Ser His Ala Phe His Ser Pro His Met Asp Ala Met
770 775 780

Leu Gly Asp Phe Arg Arg Ala Ala Glu Gln Val Thr Phe Ser Ala Pro
785 790 795 800

Arg Ile Pro Val Val Ser Asn Val Thr Gly Ala Pro Leu Pro Ala Glu
805 810 815

Thr Met Cys Thr Pro Asp Tyr Trp Val Glu His Ala Arg Ser Thr Val
820 825 830

Arg Phe Ala Asp Gly Ile Ser Trp Leu Gln Glu Gln Gly Val Thr Thr
835 840 845

Cys Leu Glu Ile Gly Pro Asp Gly Thr Leu Ser Ala Leu Ala Gln Asp
850 855 860

Ser Leu Ser Ala Pro Ala Arg Ala Ile Pro Ala Leu Arg Pro Asp Gln
865 870 875 880

Pro Glu Ala Arg Ser Val Met Thr Ala Leu Ala Glu Leu Phe Val Ala
885 890 895

Gly Thr Ala Val Glu Trp Ala Gly Val Phe Glu Gly Thr Ala Arg Glu
900 905 910

Val Gly Asp Gly Cys Gly Val Glu Leu Pro Thr Tyr Ala Phe Glu Arg
915 920 925

Glu Arg Phe Trp Leu Asp Val Glu Glu Gly Ser Ala Gly Gly Ser Gly
930 935 940

Val Ser Gly Met Trp Gly Gly Pro Leu Trp Glu Ala Val Glu Cys Gly
945 950 955 960

Asp Ala Gly Val Val Ala Ser Leu Leu Gly Val Asp Glu Gly Ala Ser
 965 970 975

Leu Gly Ala Val Val Ser Ala Leu Gly Glu Trp Gly Arg Val Arg His
 980 985 990

Glu Arg Glu Val Val Asp Gly Trp Arg Tyr Arg Glu Val Trp Arg Pro
 995 1000 1005

Val Ser Gly Gly Gly Val Gly Gly Leu Ser Gly Ala Trp Leu Val Val
 1010 1015 1020

Ser Glu Gly Glu Ala Gly Pro Val Asp Val Val Ala Glu Gly Leu Glu
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Arg Cys Gly Ala Arg Val Val Arg Val Glu Val Glu Ala Gly Cys Val
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Ser Arg Glu Val Leu Ala Gly His Leu Arg Glu Ala Val Asp Gly Glu
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Ala Val Gly Gly Val Val Ser Leu Val Gly Trp Gly Ser Gly Val Val
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Gln Ala Gly Val Ala Ser Val Gly Leu Val Gln Ala Leu Gly Asp Val
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Gly Val Gly Ala Arg Leu Trp Cys Val Thr Gly Gly Ala Val Ser Val
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Gly Gly Arg Asp Ala Val Trp Gly Pro Ala Ser Gly Val Val Trp Gly
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Leu Gly Arg Val Val Gly Ala Glu Ala Pro Asp Arg Trp Gly Gly Leu
 1140 1145 1150

Val Asp Val Pro Glu Leu Val Asp Glu Arg Val Val Asp Gly Leu Val

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1165

Gly Val Leu Ala Gly Val Gly Gly Gly Gly Glu Ser Glu Phe Ala Val

1170

1175

1180

Arg Ser Ser Gly Ala Phe Val Arg Arg Leu Val Arg Ala Pro Leu Glu

1185

1190

1195

1200

Glu Ala Val Ala Glu Arg Glu Trp Arg Pro Arg Gly Thr Val Leu Val

1205

1210

1215

Thr Gly Gly Thr Gly Glu Leu Gly Ala His Val Ala Arg Trp Met Ala

1220

1225

1230

Arg Arg Gly Ala Glu His Leu Leu Leu Val Ser Arg Arg Gly Glu Ser

1235

1240

1245

Ala Gln Gly Val Glu Glu Leu Arg Ala Asp Leu Met Gly Leu Gly Ala

1250

1255

1260

Arg Val Ser Val Val Ala Cys Asp Ala Ala Asp Arg Glu Ala Leu Ala

1265

1270

1275

1280

Glu Val Leu Arg Ser Ala Val Pro Ala Glu Cys Pro Leu Gly Val Val

1285

1290

1295

Val His Ala Ala Gly Val Val Asp Asp Gly Val Leu Glu Gly Leu Ser

1300

1305

1310

Ser Glu Arg Val Thr Gly Val Leu Arg Ala Lys Ala Leu Ala Ala Trp

1315

1320

1325

Asn Leu His Glu Leu Thr Arg Gly Ala Asp Leu Ser Gly Phe Val Val

1330

1335

1340

Phe Ser Ser Ala Ala Ala Thr Phe Gly Pro Ala Gly Gln Gly Ser Tyr

1345

1350

1355

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Ala Ala Ala Asn Ala Tyr Val Glu Ala Ile Val Arg His Arg Arg Gly
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Glu Gly Leu Pro Gly Leu Ala Val Ala Trp Gly Pro Trp Ala Gly Gly
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Gly Met Ala Glu Gly Ala Val Gly Gln Met Arg Arg Arg Gly Leu Ala
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Ala Met Thr Pro Glu Thr Ala Leu Val Ala Leu Gly Gln Ala Leu Asp
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His Asp Glu Thr Cys Val Thr Val Ala Asp Ile Asp Trp Asp Arg Phe
1425 1430 1435 1440

Thr Ala Asn Ser Leu Pro Gly Ser Arg Leu Ser Pro Leu Ile Ser Asp
1445 1450 1455

Ile Pro Glu Ala Arg Leu Ala Arg Glu Thr Thr Gly Leu Asp Thr Ala
1460 1465 1470

Thr Ala Ser Pro Asp Ser Phe Ser Ala Arg Leu Lys Ala Met Asp Thr
1475 1480 1485

Ala Glu Gln Glu Arg Ala Leu Leu Asp Leu Val Arg Thr Tyr Ala Ala
1490 1495 1500

Thr Val Leu Gly His Ser Thr Pro Thr Ala Val Arg Pro Glu Arg Ala
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Phe Arg Asp Leu Gly Phe Val Ser Val Ser Ala Val Glu Leu Arg Asn
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Arg Leu Asn Ala Val Thr Gly Leu Leu Leu Pro Thr Thr Leu Ile Phe
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Asp Tyr Pro Thr Pro Ser Ala Leu Ala Gly Tyr Leu Lys Glu Gln Leu
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Glu Glu Gly Ala Gly Gly Gln Arg Asp Ile Ala Pro Pro Val Pro Ala
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Ser Arg Val Asp Val Asp Glu Pro Ile Ala Ile Val Gly Met Ala Cys
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Arg Phe Pro Gly Gly Val Glu Ser Ala Glu Asp Leu Trp Glu Leu Val
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Ala Ser Gly Arg Asp Ala Val Gly Glu Phe Pro Val Asp Arg Gly Trp
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Asp Val Glu Ala Phe Tyr Asp Pro Glu Pro Gly Arg Ala Gly Ser Ser
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Tyr Thr Arg Arg Gly Gly Phe Leu Glu Gly Ala Ala Glu Phe Asp Ala
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Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln
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Gln Arg Leu Met Leu Glu Val Ser Trp Glu Ala Leu Glu Arg Ala Gly
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Ile Asp Pro Ala Thr Leu Arg Gly Ser Thr Thr Gly Val Phe Ala Gly
1700 1705 1710

Met Cys Ser Gln Asp Tyr Ala Asp Leu Val Arg Arg Ala Thr Glu Asp
1715 1720 1725

Leu Glu Gly Tyr Ala Met Thr Gly Leu Ser Ser Ser Val Thr Ser Gly
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Arg Val Ala Tyr Thr Leu Gly Leu Glu Gly Pro Ala Val Thr Val Asp
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Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala

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Met Ser Thr Pro Gly Ala Phe Val Glu Phe Ser Arg Gln Arg Gly Leu		
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Ser Pro Asp Gly Arg Cys Lys Ala Tyr Gly Ser Gly Ala Asp Gly Val		
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Gly Trp Ala Glu Gly Val Gly Val Leu Leu Val Glu Arg Leu Ser Glu		
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Ala Glu Arg Arg Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala		
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Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro		
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Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Cys Ala Gly Leu Ser		
1875	1880	1885
Val Ala Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr Thr Leu		
1890	1895	1900
Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Gly		
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Arg Ser Gly Glu Arg Pro Val Trp Leu Gly Ser Val Lys Ser Asn Ile		
1925	1930	1935
Gly His Ala Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val		
1940	1945	1950
Met Ala Leu Arg Ala Gly Val Leu Pro Arg Thr Leu His Val Asp Glu		
1955	1960	1965

Pro Ser Ser Gln Val Asp Trp Ser Ser Gly Ser Val Arg Val Leu Ala
1970 1975 1980

Asp Glu Val Glu Trp Pro Gly Val Glu Gly Arg Leu Arg Arg Ala Gly
1985 1990 1995 2000

Val Ser Ala Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu
2005 2010 2015

Glu Ala Ser Gly Gly Ala Asp Gly Gly Ala Gly Arg Leu Gln Glu Leu
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Gly Pro Gly Val Val Ser Gly Ser Gly Val Val Pro Trp Val Val Ser
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Ala Arg Ser Glu Leu Ala Leu Arg Gly Gln Ala Arg Arg Leu Arg Gly
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Val Val Ala Val Gly Gly Gly Ala Asp Gly Val Gly Val Ser Pro Ala
2065 2070 2075 2080

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Ala Val Val Val Ala Glu Asp Arg Asp Glu Phe Leu His Ala Leu Asp
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Thr His Trp Glu Gly Met Ala Gln Glu Leu Leu Gly Ser Ser Pro Val
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Phe Ala Gln Gln Met Ser Asp Cys Ala Gln Ala Leu Glu Pro Tyr Leu
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Asp Trp Ser Leu Leu Asp Val Leu Arg Gly Ala Pro Asp Ala Pro Pro
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Leu Gln Arg Val Asp Val Val Gln Pro Val Leu Phe Ala Val Met Val
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Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Val His Pro Asp Ala Val
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Ala Gly His Ser Gln Gly Glu Ile Ala Ala Ala Tyr Val Ala Gly Ala
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Val Glu Lys Leu Glu Pro Arg Leu Ala Thr Trp Gly Asp Arg Leu Val
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Ala Ile Gln Gly Arg Leu Leu Glu Leu Leu Ala Pro Ile Arg Ala Arg
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Gly Thr Glu Leu Asp Ala Asp Tyr Trp Tyr Arg Asn Leu Arg Gln Val

2370

2375

2380

Val Arg Phe Arg Asp Ala Thr Gln Ala Leu Val Arg Ala Gly His Thr
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Tyr Ala Phe Glu Arg Glu Arg Phe Trp Leu Asp Val Glu Gly Ala Pro
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Arg Gly Ser Gly Val Ser Gly Gln Trp Gly Gly Gln Leu Ser Glu Ala
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Ala Ala Ala Val Leu Gly His Gly Thr Ala Asp Ala Val Val Pro Glu
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Gly Val Phe Ala Gly Val Ser Gln Gln Asp Tyr Ala Glu Leu Leu Arg
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Arg Gly Thr Gln Asp His Glu Gly Tyr Ala Leu Thr Gly Val Ser Asn
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Cys Ala Gly Leu Ser Val Ala Asp Val Asp Val Val Glu Gly His Gly
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Thr Tyr Gly Gln Gly Arg Ser Gly Glu Arg Pro Val Trp Leu Gly Ser
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Val Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala Gly Val Ala Gly

2980

2985

2990

Val Ile Lys Met Val Met Ala Leu Asn His Glu Leu Leu Pro Thr Ser

2995

3000

3005

Leu His Ile Asp Glu Pro Ser Pro His Ile Asp Trp Ser Ser Gly Gly

3010

3015

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Val Arg Leu Leu Thr Glu Pro Val Pro Trp Gln Gln Asn Gly Arg Pro

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Arg Arg Ala Gly Val Ser Ala Phe Gly Val Ser Gly Thr Asn Ala His

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Val Ile Ile Glu Gln Ala Pro Val Glu Ala His Val Ile Ser Glu Pro

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Val Pro Ala Glu Ala His Val Ile Val Glu Gln Ala Pro Val Glu Ala

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Pro His Val Val Asp Ala Thr Gly Pro Ala Asp Leu Thr Glu Pro Gln

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Glu Glu Ala Ala Glu Pro Glu Cys Val Ala Asp Ala Val Thr Glu Met

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3110

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3120

Ser Ala Glu Pro Glu Cys Val Ala Asp Ala Met Ser Glu Met Ser Ala

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Glu Cys Val Ala Glu Ala Val Ser Asp Lys Ser Ala Glu Pro Glu Cys

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Val Ala Asp Ala Met Ser Asp Lys Pro Ala Leu Leu Pro Ile Pro Trp

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3165

Leu Leu Ser Ala Lys Ser Glu Arg Ala Leu Arg Gly Gln Ala Arg Arg

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Leu Arg Gln Phe Ala Ala Arg Ala Ser Asp Ala Arg Pro Ala Asp Val

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Ala His Pro Ala Tyr Ala Asp Ala Leu Asp Gln Val Leu Ala Glu Leu
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Asp Gly His Leu Asp Gln Pro Leu Arg Pro Leu Ile His Ala Ser Ala
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Asp Leu Ala Asp Val Ala Asp Ala Ala Asp Val Leu Asp Arg Thr Arg
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Tyr Ala Gln Pro Ala Leu Phe Ala Val Gln Val Ala Leu Phe Arg His
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Leu Glu Arg Leu Gly Val Arg Ala Asp Phe Val Ala Gly His Ser Ile
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Gly Glu Leu Ala Ala Ala His Val Ala Gly Val Leu Pro Leu Ala Ala
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3380 3385 3390

Pro Gly Gly Ala Met Val Ala Val Arg Ala Ser Glu Ala Glu Ala Arg
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Gln Ala Leu Asp Gly Arg Glu Ala Arg Val Ser Val Ala Ala Val Asn
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Gly Pro Ala Ser Val Val Phe Ser Gly Ala Glu Asp Glu Val Gly Asn
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Met Ala Asp Trp Phe Ala Glu Arg Gly Arg Arg Val Lys Arg Leu Arg
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Thr Gly His Ala Phe His Ser Pro Leu Met Asp Pro Met Leu Glu Glu
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Phe Gln Gln Val Ala Ala Ser Leu Thr Tyr Ser Glu Pro Ala Ile Pro
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Met Val Ser Thr Leu Thr Gly Asp Ile Val Ala Ala Gly Glu Leu Ser
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Asp Pro Glu Tyr Trp Val Arg Gln Val Arg Arg Thr Val Arg Phe Gly
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Asp Ala Ile Ser Arg Leu His Thr Asp Gly Val Arg Thr Phe Met Glu
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Leu Gly Pro Asp Gly Thr Leu Ser Ala Leu Ala Glu Glu Cys Leu Glu
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Ala Thr Ala Asp Ser His Pro Ala Asp Asp Asp Thr Gly Thr Pro Gln
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Glu Asn Leu Leu Ile Pro Leu Leu Arg Pro Asp Ser Pro Glu Pro Gly
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Thr Leu Leu Thr Gly Leu Ala Arg Leu His Thr His Gly Ala Ala Ala
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Val Asn Trp Pro Ala Ala Leu Pro Glu Arg Asp Arg Ala Arg His Leu
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Asp Leu Pro Thr Tyr Ala Phe Asp His His Arg Tyr Trp Val Asp Thr
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Ser Ala Gly His Pro Gly Asp Leu Ser Ala Ala Gly Leu Gly Thr Ala
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Gly His Pro Leu Leu Gly Ser Ala Val Ala Leu Ala Glu Ser Gln Glu
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Leu Leu Phe Thr Gly Arg Leu Ser Leu Arg Thr His Pro Trp Leu Ala
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Asp His Ala Ile Phe Gly Thr Val Leu Leu Pro Gly Thr Ala Ile Leu
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Glu Leu Ala Val Arg Ala Gly Asp Glu Val Asp Cys Gly Thr Val Glu
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Ile Leu Gln Leu Ser Val Gly Ala Pro Gln Gly Pro Gln Thr Pro Glu
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Glu Pro Glu Arg Arg Thr Phe Ala Leu Tyr Ala Arg Glu Asp Asp Gly
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Leu Ser Ser Ser Ser Ala Ala Ala Thr Gly Thr Glu Trp Thr Cys His
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Ala Thr Gly Val Leu Thr Gly Thr Ala Arg Pro Ala Glu Glu His Thr
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Gln Glu Pro Trp Pro Pro Ala Asp Ala Ala Pro Val Asp Leu Asp Gly

3795

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3805

Trp Tyr Glu Gln Leu Ala Gly Ala Gly Leu Gly Tyr Gly Pro Val Phe
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Gln Gly Leu Arg Glu Val Trp Arg Arg Gly Asp Glu Val Phe Ala Val
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Val Thr Leu Pro Glu Ser Thr Glu Gly Gln Ala Ala Asp Ala Ala Arg
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Tyr Ala Leu His Pro Ala Leu Leu Asp Ala Ala Leu His Pro Val Val
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Leu Arg His Glu Gly Asp Ala Ala Ala Asp Gly His Gly Trp Leu Pro
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Phe Ser Trp Thr Gly Val Thr Val Ala Ala Ser Gly Ala Ser Thr Leu
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His Val Arg Leu Thr Val Arg Thr Asp Glu Asp Ala Val Gly Leu Leu
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Ala Thr Asp Ala Ser Gly Arg Ile Val Ile Ser Ala Gly Ser Leu Ala
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Phe Arg Pro Val Ser Ala Glu Gln Leu Gln Ala Ala Arg Thr Gly Tyr
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His Asp His Leu Phe Arg Ile Glu Trp Arg Pro Leu His Leu Pro Thr
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Thr Pro Ala Arg Thr Ala Asp Trp Ala Leu Ile Gly Pro Gly Ala Arg
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Arg His Leu Leu Leu Ala Thr Arg Arg Gly Thr Ala Ala Asp Gly Ala
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Ala Asp Leu Val Ala Glu Leu Ala Gly Leu Gly Ala Glu Ala Thr Val
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Ala Ala Cys Asp Ile Gly Asp Arg Ala Ala Val Ala Ala Leu Leu Asp
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Gln Val Pro Ala Gln His Pro Leu Lys Ala Val Ile His Thr Ala Gly
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Val Val Asp Asp Gly Ile Leu Thr Ser Leu Thr Pro Glu Arg Met Glu
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Ala Val Leu His Ala Lys Ala Phe Gly Ala Ala His Leu His Asp Leu
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Thr Arg Asp Ala Gly Leu Thr Thr Phe Thr Val Phe Ser Ser Ala Ala
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Ala Ser Phe Gly Ser Pro Gly Gln Gly Asn Tyr Thr Ala Ala Asn Ala
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Phe Leu Asp Ala Leu Met Gln His Arg His Thr Gln Ala Leu Pro Gly
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Arg Ser Leu Ala Trp Gly Leu Trp Gly Glu Ala Asp Gly Met Thr Arg
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Asn Leu Ala Gly Thr Asp Phe Ala Arg Met Ala Arg Gly Gly Leu Leu
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Pro Leu Ser Asn Ala Gln Gly Leu Ala Leu Leu Asp Thr Ala Asp Arg
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Leu Gly Pro Phe Gly Asp Gly Leu Leu Leu Ala Thr Arg Leu Asp Ala

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Ala Thr Leu His Ala Gln Ala Thr Ala Gly Ala Leu Pro Arg Ile Leu
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His Gly Leu Ile Arg Ile Pro Ala Arg Arg Ser Ala Asp His Gly Ile
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Ala Thr Asp Thr Pro Ala Thr Leu Arg Glu Arg Leu Ala Gly Leu Thr
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Ile Pro Ala Gln Arg Thr Gly Leu Leu Leu Glu Leu Val Arg Thr His
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Ala Ala Ala Val Leu Gly His Pro Thr Ser Ala Val Thr Ala Ala Asp
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Gly Ala Leu Pro Asp Asp Leu Val Pro Ala Asp Thr Glu Phe Arg Asp
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Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu Arg Asn Arg Ile Asn
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Ala Val Thr Gly Leu Arg Leu Pro Ala Thr Leu Ile Phe Asp Gln Pro
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Ser Pro Ala Ala Leu Ala Asp His Leu Ala Thr Arg Leu Thr Ala Glu
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Ala Gly Thr Pro Asp Glu Pro Ala Pro Ala Ala Ala Ala Ala Gly Ala
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Gly Ser Ala Gly Ser Ala Glu Thr Gly Gln Gln Arg Ser Thr Gly Ser
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Glu Lys Gln Gln Thr Arg Gly Gly Thr Ser Thr Glu Thr Val Glu Ser
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Leu Phe Trp Ile Gly His Asp Thr Arg Arg Ile Glu Glu Ser Met Ala
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Leu Leu Ser Ala Ala Ser Phe Phe Arg Pro Ala Phe Thr Asp Pro Ser
4625 4630 4635 4640

Asp Ile Pro Glu Pro Thr Phe Val Arg Leu Ala Gln Gly Glu Ala Arg
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Ala Gln Gly Glu Ala Leu Ala Arg Gly Glu Thr Arg Pro Ala Leu Ile
4660 4665 4670

Cys Leu Pro Thr Val Ala Ala Val Ser Ser Val Tyr Gln Tyr Ser Arg
4675 4680 4685

Phe Ala Ala Gly Leu Asn Gly His Arg Asp Val Trp Tyr Val Pro Ala
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Pro Gly Phe Leu Glu Gly Glu Pro Leu Pro Ser Gly Ile Gly Ala Val
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Thr Arg Met Phe Ala Asp Ala Ile Val Arg Phe Thr Asp Gly Ala Pro
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Phe Ala Leu Ala Gly His Ser Ala Gly Gly Trp Phe Val Tyr Ala Val
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Thr Ser His Leu Glu Arg Leu Gly Val Arg Pro Glu Ala Val Val Thr
4755 4760 4765

Met Asp Ala Tyr Leu Pro Asp Asp Gly Ile Ala Pro Val Ala Ser Ala
4770 4775 4780

Leu Thr Ser Glu Ile Phe Asp Arg Val Thr Gln Phe Val Asp Val Asp
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Tyr Thr Arg Leu Val Ala Met Gly Gly Tyr Phe Arg Ile Phe Ser Gly
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Asp Gly Glu Gln Met Pro Pro Pro Trp Gly Val Pro His Thr Val Leu
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Asp Ile Gln Gly Asn His Phe Thr Met Leu Glu Gln Phe Ala Asp Ser
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Thr Ala Arg His Val Asp Glu Trp Leu Thr Glu Ile Ala Ser Val Arg
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<212> PRT

<213> Streptomyces avermitilis

<400> 6

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Met Glu Ala Ser Ser Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg
35 40 45

Phe Pro Gly Gly Val Cys Ser Pro Glu Glu Leu Trp Glu Leu Val Ala
50 55 60

Ser Gly Gly Asp Ala Ile Gly Glu Phe Pro Ala Gly Arg Gly Trp Asp
65 70 75 80

Leu Glu Gly Leu Phe Asp Ser Asp Pro Asp Arg Ser Gly Thr Ser Tyr

85

90

95

Ala Arg Tyr Gly Gly Phe Leu Tyr Glu Ala Gly Glu Phe Asp Ala Asp
 100 105 110

Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln
 115 120 125

Arg Leu Leu Leu Glu Thr Ser Trp Glu Ala Phe Glu Arg Ala Gly Ile
 130 135 140

Asp Pro Leu Ser Met Arg Gly Ser Arg Thr Gly Val Phe Ala Gly Val
 145 150 155 160

Met Tyr His Asp Tyr Gly Ser Arg Leu Gly Thr Ile Pro Glu Gly Phe
 165 170 175

Glu Gly Tyr Ile Gly Asn Gly Ser Gly Gly Ala Val Ala Ser Gly Arg
 180 185 190

Val Ala Tyr Thr Leu Gly Leu Glu Gly Pro Ala Val Ser Val Asp Thr
 195 200 205

Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ser Leu
 210 215 220

Arg Ser Gly Glu Cys Thr Leu Ala Leu Ala Gly Gly Val Thr Val Met
 225 230 235 240

Ser Thr Pro His Leu Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ser
 245 250 255

Val Asp Gly Arg Cys Lys Ser Phe Ala Gly Gly Ala Asp Gly Thr Gly
 260 265 270

Met Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala
 275 280 285

Val Arg Leu Gly His Arg Val Leu Ala Val Leu Arg Gly Ser Ala Val
290 295 300

Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ala
305 310 315 320

Gln Glu Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Ser Val
325 330 335

Ala Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly
340 345 350

Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Arg Ala
355 360 365

Gly Asn Arg Pro Leu Trp Leu Gly Ser Val Lys Ser Asn Ile Gly His
370 375 380

Ala Gln Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala
385 390 395 400

Leu Arg Glu Gly Val Leu Pro Arg Thr Leu His Val Asp Glu Pro Ser
405 410 415

Pro Gln Val Asp Trp Ser Ala Gly Ala Val Arg Leu Leu Thr Glu Ala
420 425 430

Val Pro Trp Pro Gly Asp Ala Ala Gly Arg Leu Arg Arg Ala Gly Val
435 440 445

Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu
450 455 460

Ala Pro Ala Ala Gly Gly Cys Val Ala Gly Gly Gly Val Leu Glu Gly
465 470 475 480

Ala Pro Gly Leu Ala Ile Ser Val Ala Glu Ser Val Ala Ala Pro Val
485 490 495

Ala Val Ser Ala Pro Val Ala Glu Ser Val Pro Val Pro Val Pro Val
500 505 510

Pro Val Pro Val Pro Val Ser Ala Arg Ser Glu Ala Gly Leu Arg Ala
515 520 525

Gln Ala Glu Ala Leu Arg Gln Tyr Val Ala Val Arg Pro Asp Val Ser
530 535 540

Leu Ala Asp Val Gly Ala Gly Leu Ala Cys Gly Arg Ala Val Leu Glu
545 550 555 560

His Arg Ala Val Val Leu Ala Ala Asp Arg Glu Glu Leu Val Gln Gly
565 570 575

Leu Gly Ala Leu Ala Ala Gly Glu Pro Asp Arg Arg Val Thr Thr Gly
580 585 590

His Ala Pro Gly Gly Asp Arg Gly Gly Val Val Phe Val Phe Pro Gly
595 600 605

Gln Gly Gly Gln Trp Ala Gly Met Gly Val Arg Leu Leu Ala Ser Ser
610 615 620

Pro Val Phe Ala Arg Arg Met Gln Ala Cys Glu Glu Ala Leu Ala Pro
625 630 635 640

Trp Val Asp Trp Ser Val Val Asp Ile Leu Arg Arg Asp Ala Gly Asp
645 650 655

Ala Val Trp Glu Arg Ala Asp Val Val Gln Pro Val Leu Phe Ser Val
660 665 670

Met Val Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Ile Glu Pro Asp
675 680 685

Ala Val Leu Gly His Ser Gln Gly Glu Ile Ala Ala Ala His Val Cys

690

695

700

Gly Ala Leu Ser Leu Lys Asp Ala Ala Lys Thr Val Ala Leu Arg Ser
705 710 715 720

Arg Ala Leu Ala Ala Val Arg Gly Arg Gly Gly Met Ala Ser Val Pro
725 730 735

Leu Pro Ala Gln Glu Val Glu Gln Leu Ile Gly Glu Arg Trp Ala Gly
740 745 750

Arg Leu Trp Val Ala Ala Val Asn Gly Pro Arg Ser Thr Ala Val Ser
755 760 765

Gly Asp Ala Glu Ala Val Asp Glu Val Leu Ala Tyr Cys Ala Gly Thr
770 775 780

Gly Val Arg Ala Arg Arg Ile Pro Val Asp Tyr Ala Ser His Cys Pro
785 790 795 800

His Val Gln Pro Leu Arg Glu Glu Leu Leu Glu Leu Leu Gly Asp Ile
805 810 815

Ser Pro Gln Pro Ser Gly Val Pro Phe Phe Ser Thr Val Glu Gly Thr
820 825 830

Trp Leu Asp Thr Thr Thr Leu Asp Ala Ala Tyr Trp Tyr Arg Asn Leu
835 840 845

His Gln Pro Val Arg Phe Ser Asp Ala Val Gln Ala Leu Ala Asp Asp
850 855 860

Gly His Arg Val Phe Val Glu Val Ser Pro His Pro Thr Leu Val Pro
865 870 875 880

Ala Ile Glu Asp Thr Thr Glu Asp Thr Ala Glu Asp Val Thr Ala Ile
885 890 895

Gly Ser Leu Arg Arg Gly Asp Asn Asp Thr Arg Arg Phe Leu Thr Ala
 900 905 910

Leu Ala His Thr His Thr Thr Gly Ile Gly Thr Pro Thr Thr Trp His
 915 920 925

His His Tyr Thr His His His Thr His Pro His Asn His His Leu Asp
 930 935 940

Leu Pro Thr Tyr Pro Phe Gln Arg Gln His Tyr Trp Leu Asp Ala Pro
 945 950 955 960

Thr Gly Ala Gly Asp Val Ala Ala Ala Gly Leu Glu Pro Ala Glu His
 965 970 975

Pro Leu Leu Ala Ala Thr Val Gln Leu Ala Asp Thr Asp Gly Cys Leu
 980 985 990

Leu Thr Gly Arg Leu Ser Leu Arg Ser His Pro Trp Leu Gly Asp Tyr
 995 1000 1005

Glu Val Gly Gly Ala Val Leu Leu Ser Gly Ser Ala Phe Val Glu Leu
 1010 1015 1020

Ala Val Gln Val Gly Glu Arg Val Gly Cys Thr Arg Ile Glu Gln Leu
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Thr Val His Ala Pro Leu Val Val Pro Val Gly Gly Gly Val Ser Val
 1045 1050 1055

Gln Val Gly Val Ala Ala Ala Asp Gly Glu Gly Arg Arg Leu Val Ser
 1060 1065 1070

Val Tyr Ala Arg Gly Gly Ser Ala Cys Gly Gly Gly Gly Ala Ser Gly
 1075 1080 1085

Gly Val Trp Thr Cys His Ala Ser Gly Val Leu Val Glu Ala Ala Ala
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Gly Gly Gly Val Val Val Asp Gly Leu Ala Gly Val Trp Pro Pro Arg
1105 1110 1115 1120

Gly Ala Val Ala Val Asp Val Asp Gly Val Arg Asp Arg Leu Ala Gly
1125 1130 1135

Ala Gly Cys Val Leu Gly Pro Val Phe Ser Gly Leu Arg Ala Val Trp
1140 1145 1150

Arg Asp Gly Gly Asp Leu Leu Ala Glu Val Cys Leu Pro Glu Glu Ala
1155 1160 1165

Trp Gly Asp Ala Ala Gly Phe Gly Leu His Pro Ala Leu Leu Asp Gly
1170 1175 1180

Val Val Gln Pro Leu Ser Val Leu Leu Pro Gly Gly Thr Gly Phe Gly
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Glu Gly Ala Gly Phe Gly Glu Gly Val Arg Val Pro Ala Val Trp Gly
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Gly Val Ser Leu His Arg Ala Gly Val Thr Gly Val Arg Val Arg Val
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Trp Ala Val Gly Arg Gly Gly Gly Arg Glu Ala Val Ser Val Val Val
1235 1240 1245

Gly Asp Glu Ala Gly Val Pro Val Ala Ser Val Asp Arg Leu Glu Leu
1250 1255 1260

Arg Pro Val Asp Met Gly Gln Leu Arg Ala Val Ser Val Ser Ala Gly
1265 1270 1275 1280

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Pro Val Cys Gly Gln Ala Trp Ala Trp His Glu Asp Val Gly Glu Ser

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09914286 082441
F04280 982441

1300

1305

1310

Gly Gly Gly Pro Val Pro Gly Val Val Val Leu Arg Cys Pro Asp Ala
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Gly Ala Gly Gly Gly Gly Gly Gly Gly Val Gly Glu Val Val Gly Gly
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Val Leu Gly Val Val Gln Gly Trp Leu Gly Leu Glu Arg Phe Ala Gly
1345 1350 1355 1360

Ser Arg Leu Val Val Val Thr Arg Gly Ala Val Val Ala Gly Gln Glu
1365 1370 1375

Asp Gly Pro Val Asp Val Val Gly Ala Ala Val Trp Gly Leu Val Arg
1380 1385 1390

Ser Ala Gln Ala Glu His Pro Asp Arg Phe Val Leu Leu Asp Leu Asp
1395 1400 1405

Thr Asp Thr Asp Thr Gly Thr Asp Leu Asp Thr Gly Ala Gly Ala Gly
1410 1415 1420

Ala Gly Ala Gly Trp Gly Val Asp Gly Gly His Val Ala Ala Val Val
1425 1430 1435 1440

Ala Cys Gly Glu Pro Gln Leu Ala Val Arg Gly Glu Arg Val Leu Ala
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Ala Arg Leu Thr Arg Leu Glu Ser Ser Val Asp Val Pro Ala Gln Arg
1460 1465 1470

Ser Gly Asp Val Ala Gly Arg Glu Val Leu Pro Trp Leu Ser Gly Gly
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Ser Val Leu Val Thr Gly Gly Thr Gly Val Leu Gly Ala Ala Val Ala
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Arg His Leu Ala Gly Val Cys Gly Val Arg Asp Leu Leu Leu Val Ser
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Arg Arg Gly Pro Asp Ala Pro Gly Ala Glu Gly Leu Arg Ala Glu Leu
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Ala Ala Leu Gly Ala Glu Val Arg Ile Val Ala Cys Asp Val Gly Glu
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Arg Arg Glu Val Val Arg Leu Leu Glu Gly Val Pro Ala Gly Cys Pro
1555 1560 1565

Leu Thr Gly Val Val His Ala Ala Gly Val Leu Asp Asp Ala Thr Ile
1570 1575 1580

Ala Ser Leu Thr Pro Glu Arg Leu Gly Thr Val Phe Ala Ala Lys Val
1585 1590 1595 1600

Asp Ala Ala Leu Leu Leu Asp Glu Leu Thr Arg Gly Met Glu Leu Ser
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Ala Phe Val Leu Phe Ser Ser Ala Ala Gly Ile Leu Gly Ser Ala Gly
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Gln Gly Asn Tyr Ala Ala Ala Asn Ala Ala Leu Asp Ala Leu Ala Tyr
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Trp Glu Glu Ala Ser Gly Met Thr Gly His Leu Ala Gly Thr Asp His
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1685 1690 1695

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Gly Ala Asp Asn Gly Ala Gln Leu His Ala Arg Leu Ala Gly Gln Thr
1745 1750 1755 1760

His Glu Gln Gln His Thr Thr Leu Leu Ala Leu Val Arg Ser His Ile
1765 1770 1775

Ala Thr Val Leu Gly His Thr Thr Pro Asp Thr Ile Pro Pro Asp Arg
1780 1785 1790

Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu Arg
1795 1800 1805

Asn Arg Leu Ser Arg Thr Thr Gly Leu Arg Leu Pro Thr Thr Leu Ala
1810 1815 1820

Phe Asp His Pro Asn Pro Thr Thr Leu Thr His His Leu His Thr Gln
1825 1830 1835 1840

Leu Leu Gly Ser Asp Ser Thr Ala Ser Ile Pro Ala Pro Arg Ala Ala
1845 1850 1855

Ala Val Pro Ala Asp Gln Asp Glu Pro Val Ala Ile Ile Gly Met Ala
1860 1865 1870

Cys Arg Tyr Pro Gly Gly Val Thr Ser Ala Glu Glu Leu Trp Glu Leu
1875 1880 1885

Leu Ala Ser Gly Arg Asp Thr Val Gly Glu Phe Pro Thr Asp Arg Gly
1890 1895 1900

Trp Asp Leu Glu Ala Leu Phe Asp Pro Glu Pro Gly Arg Pro Gly Thr

1905 1910 1915 1920

Ser Tyr Thr Arg Cys Gly Ser Phe Leu Tyr Asp Ala Gly Glu Phe Asp
1925 1930 1935

Ala Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro
1940 1945 1950

Gln Gln Arg Leu Leu Leu Glu Ala Ser Trp Glu Ala Met Glu Gln Ala
1955 1960 1965

Gly Ile Asp Pro Thr Thr Val Arg Gly Ser Gln Thr Gly Val Phe Ala
1970 1975 1980

Gly Leu Ile Pro Gln Ala Tyr Gly Pro Arg Leu His Glu Asn Ala Ala
1985 1990 1995 2000

Ala Asp Thr Glu Gly Tyr Val Leu Thr Gly Thr Ser Gly Ser Val Ala
2005 2010 2015

Ser Gly Arg Ile Ser Tyr Thr Phe Gly Phe Glu Gly Pro Ala Val Ser
2020 2025 2030

Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys
2035 2040 2045

Gln Ala Leu Arg Ala Gly Glu Cys Ser Met Ala Leu Ala Gly Gly Val
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Thr Val Met Ser Ser Pro Gly Ala Phe Val Glu Phe Ser Arg Gln Arg
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Gln Asp Arg Ala Gly Glu Gly Pro Leu Trp Leu Gly Ser Val Lys Ser
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Asp Glu Pro Ser Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu
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Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly

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Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala

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Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro

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Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His His

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Ile Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro

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Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr

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His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His

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Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile

2645

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2655

Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr

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Gln Gln Ala Arg Asn Thr Val Asp Ile Ala Thr Thr Thr Gln Thr Leu

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2680

2685

His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr

2690

2695

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Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Thr Pro Thr Thr Thr

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2715

2720

Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu Thr
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Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr His
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His His Asn Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr
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Pro Phe Gln His His His Tyr Trp Leu Glu Ser Thr Gln Pro Gly Ala
2770 2775 2780

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Arg Leu Ser Leu Arg Thr His Pro Trp Leu Ala Gly His Ala Val Gly
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Gly Val Val Leu Leu Pro Gly Thr Ala Phe Ala Glu Leu Ala Leu His
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Asp Asp Ile Leu Val Glu Ala Arg Leu Pro Glu Glu Val Ser Gly Asp
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Ala Ala Ala Tyr Gly Leu His Pro Ala Leu Leu Asp Ala Ala Leu Gln
2995 3000 3005

Gly Thr Gly Leu Leu Ser Val Ala Gly Pro Gly Thr Pro Val Val Pro
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His Val Trp Asn Gly Leu Arg Phe Arg Thr His Gly Ala Val Ser Val
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Arg Ala Cys Leu Ser Thr Leu Gly Ala Thr Gly Ala Ala Val Cys Val
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Arg Ile Thr Asp Asp Thr Gly Val Pro Val Ala Ser Val Asp Arg Leu
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Glu Leu Arg Pro Val Asp Met Gly Gln Leu Arg Ala Val Ser Val Ser
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Ala Gly Arg Arg Gly Ser Leu Tyr Ala Val Gln Trp Ala Glu Val Gly
3090 3095 3100

Pro Val Pro Val Cys Gly Gln Ala Trp Ala Trp His Glu Asp Val Gly
3105 3110 3115 3120

Glu Ser Gly Gly Gly Pro Val Pro Gly Val Val Val Leu Arg Cys Pro

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3125

3130

3135

Asp Ala Gly Ala Asp Gly Gly Gly Gly Gly Gly Val Gly Glu Val Val
3140 3145 3150

Gly Gly Val Leu Gly Val Val Gln Gly Trp Leu Gly Leu Glu Arg Phe
3155 3160 3165

Ala Gly Ser Arg Leu Val Val Val Thr Arg Gly Ala Val Val Ala Gly
3170 3175 3180

Pro Glu Asp Gly Pro Val Asp Val Val Gly Ala Ala Val Trp Gly Leu
3185 3190 3195 3200

Val Arg Ser Ala Gln Ala Glu His Pro Asp Arg Phe Val Leu Leu Asp
3205 3210 3215

Leu Asp Thr Asp Leu Asp Ser Gly Ala Asp Ala Asp Ala Gly Asn Glu
3220 3225 3230

Ala Gly Met Gly Ser Gly Leu Asp Gly Gly Arg Val Ala Ala Val Val
3235 3240 3245

Ala Cys Gly Glu Pro Gln Leu Ala Val Arg Gly Glu Arg Val Leu Ala
3250 3255 3260

Ala Arg Leu Thr Arg Leu Glu Ser Pro Val Asp Val Ser Gly Arg Glu
3265 3270 3275 3280

Val Leu Pro Trp Leu Ser Gly Gly Ser Val Leu Val Thr Gly Gly Thr
3285 3290 3295

Gly Val Leu Gly Ala Ala Val Ala Arg His Leu Ala Gly Val Cys Gly
3300 3305 3310

Val Arg Asp Leu Leu Leu Val Ser Arg Arg Gly Pro Asp Ala Pro Gly
3315 3320 3325

Ala Glu Gly Leu Arg Ala Glu Leu Ala Ala Leu Gly Ala Glu Val Arg

3330

3335

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Ile Val Ala Cys Asp Val Gly Glu Arg Arg Glu Val Val Arg Leu Leu

3345

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3355

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Glu Gly Val Pro Ala Gly Cys Pro Leu Thr Gly Val Val His Ala Ala

3365

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3375

Gly Val Leu Asp Asp Ala Thr Ile Ala Ser Leu Thr Pro Glu Arg Leu

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Gly Thr Val Phe Ala Ala Lys Val Asp Ala Ala Leu Leu Leu Asp Glu

3395

3400

3405

Leu Thr Arg Gly Met Glu Leu Ser Ala Phe Val Leu Phe Ser Ser Ala

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3420

Ala Gly Ile Leu Gly Ser Ala Gly Gln Gly Asn Tyr Ala Ala Ala Asn

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3430

3435

3440

Ala Ala Leu Asp Ala Leu Ala Tyr Arg Arg Arg Ala Ala Gly Leu Pro

3445

3450

3455

Gly Val Ser Leu Ala Trp Gly Leu Trp Glu Glu Ala Ser Gly Met Thr

3460

3465

3470

Gly His Leu Ala Gly Thr Asp His Arg Arg Ile Ile Arg Ser Gly Leu

3475

3480

3485

His Pro Met Ser Thr Pro Asp Ala Leu Ala Leu Phe Asp Ala Ala Leu

3490

3495

3500

Ala Leu Asp Arg Pro Val Leu Leu Pro Ala Asp Leu Arg Pro Ala Pro

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3510

3515

3520

Pro Leu Pro Pro Leu Leu Gln Asp Leu Leu Pro Ala Thr Arg Arg Arg

3525

3530

3535

Thr Thr Arg Thr Thr Thr Thr Gly Gly Ala Asp Asn Gly Ala Gln Leu
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His Ala Arg Leu Ala Gly Gln Thr His Glu Gln Gln His Thr Thr Leu
 3555 3560 3565

Leu Ala Leu Val Arg Ser His Ile Ala Thr Val Leu Gly His Asn Ala
 3570 3575 3580

Pro Glu Met Ile Pro Val Asp Ser Ala Phe Arg Asp Leu Gly Phe Asp
 3585 3590 3595 3600

Ser Leu Thr Ala Val Glu Leu Arg Asn Arg Leu Gly Glu Ala Thr Gly
 3605 3610 3615

Leu Arg Leu Pro Thr Ser Leu Val Phe Asp Gln Pro Asn Ala Ala Thr
 3620 3625 3630

Leu Ala Arg His Leu Arg Arg Glu Leu Met Gly Asp Asp Ala Glu Gly
 3635 3640 3645

Glu Thr Pro Ser Gln Val Ala Leu His Gln Val Ala Ala Asp Glu Pro
 3650 3655 3660

Ile Ala Ile Val Gly Met Ala Cys Arg Phe Pro Gly Gly Val Cys Ser
 3665 3670 3675 3680

Pro Glu Glu Leu Trp Glu Leu Val Ala Ser Gly Gly Asp Ala Ile Gly
 3685 3690 3695

Glu Phe Pro Ala Gly Arg Gly Trp Asp Leu Glu Gly Leu Phe Asp Ser
 3700 3705 3710

Asp Pro Asp Arg Ser Gly Thr Ser Tyr Ala Arg Tyr Gly Gly Phe Leu
 3715 3720 3725

Tyr Glu Ala Gly Glu Phe Asp Ala Asp Phe Phe Gly Ile Ser Pro Arg
 3730 3735 3740

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 104260" 98247660

Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Thr Ser
3745 3750 3755 3760

Trp Glu Ala Phe Glu Arg Ala Gly Ile Asp Pro Leu Ser Met Arg Gly
3765 3770 3775

Ser Arg Thr Gly Val Phe Ala Gly Val Met Tyr His Asp Tyr Ala Ala
3780 3785 3790

Arg Leu His His Val Pro Glu Gly Phe Glu Gly Leu Ile Ala Asn Gly
3795 3800 3805

Ser Ala Gly Ser Val Ala Thr Gly Arg Val Ala Tyr Ser Phe Gly Leu
3810 3815 3820

Glu Gly Pro Ala Val Thr Val Asp Thr Ala Cys Ser Ser Ser Leu Val
3825 3830 3835 3840

Ala Leu His Trp Ala Ala Gln Ala Leu Arg Ala Gly Glu Cys Ser Met
3845 3850 3855

Ala Leu Ala Gly Gly Val Thr Val Met Ser Ser Pro Gly Thr Phe Val
3860 3865 3870

Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala Asp Gly Arg Cys Lys Ala
3875 3880 3885

Tyr Ser Ala Ala Ala Asp Gly Thr Gly Trp Ala Glu Gly Val Gly Met
3890 3895 3900

Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly His Arg Val
3905 3910 3915 3920

Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn
3925 3930 3935

Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln Gln Arg Val Ile Arg Gln

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T04230 98241660

3940	3945	3950
Ala Leu Ala Asn Ala Gly Leu Thr Pro Ala Asp Val Asp Ala Val Glu		
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Gly His Gly Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala		
3970	3975	3980
Leu Leu Ala Ala Tyr Gly Gln His Arg Pro His His Arg Pro Leu Trp		
3985	3990	3995 4000
Leu Gly Ser Leu Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala Gly		
4005	4010	4015
Val Gly Gly Val Ile Lys Met Val Met Ala Leu Arg Asn Gly Leu Leu		
4020	4025	4030
Pro Gln Thr Leu His Val Asp Glu Pro Thr Pro Gln Val Asp Trp Ser		
4035	4040	4045
Thr Gly Ala Val Gln Leu Leu Thr Gln Pro Val Pro Trp Pro Ala Asp		
4050	4055	4060
Pro Ala Gly Arg Pro Arg His Ala Gly Val Ser Ser Phe Gly Val Ser		
4065	4070	4075 4080
Gly Thr Asn Ala His Val Ile Leu Glu Glu Ala Pro Ala Ala Ala Gly		
4085	4090	4095
Gly Ala Ala Gly Gly Gly Val Ser Val Gly Ala Pro Asn Pro Ala Leu		
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Pro Val Ala Glu Ser Glu Pro Val Pro Val Pro Val Pro Val Ser Ala		
4115	4120	4125
Arg Ser Glu Ala Gly Leu Arg Ala Gln Ala Gln Ala Leu Arg Gln Tyr		
4130	4135	4140

Val Ala Ala Arg Pro Asp Met Ser Pro Ala Asp Ile Gly Ala Gly Leu
4145 4150 4155 4160

Ala Arg Gly Arg Ala Val Leu Glu His Arg Ala Val Ile Leu Ala Ala
4165 4170 4175

Asp Arg Glu Glu Leu Ala Gln Ala Leu Thr Ala Leu Ala Ala Gly Glu
4180 4185 4190

Pro His Pro His Ile Thr Thr Gly His Thr Arg Gly Ser Asp Arg Gly
4195 4200 4205

Gly Val Val Phe Val Phe Pro Gly Gln Gly Gly Gln Trp Ala Gly Met
4210 4215 4220

Gly Leu Thr Leu Leu Thr Ser Ser Pro Val Phe Ala Glu His Ile Asp
4225 4230 4235 4240

Ala Cys Glu Lys Ala Leu Thr Pro Trp Val Pro Trp Ser Leu Thr Asp
4245 4250 4255

Ile Leu His Arg Asp Pro Asp Asp Pro Ala Trp Gln Gln Ala Asp Val
4260 4265 4270

Val Gln Pro Val Leu Phe Ser Ile Met Val Ser Leu Ala Ala Leu Trp
4275 4280 4285

Arg Ser Tyr Gly Ile Glu Pro Asp Ala Val Leu Gly His Ser Gln Gly
4290 4295 4300

Glu Ile Ala Ala Ala His Ile Cys Gly Ala Leu Ser Leu Lys Asp Ala
4305 4310 4315 4320

Ala Lys Thr Val Ala Leu Arg Ser Gln Ala Leu Ala Ala Val Arg Gly
4325 4330 4335

Arg Gly Ala Met Val Ser Leu Pro Leu Pro Ala Gln Asp Val Gln Gln
4340 4345 4350

Leu Ile Ser Glu Arg Trp Glu Gly Gln Leu Trp Val Ala Ala Leu Asn
4355 4360 4365

Gly Pro His Ser Thr Thr Val Ser Gly Asp Thr Thr Ala Val Glu Glu
4370 4375 4380

Leu Leu Thr His Cys Ala Asp Thr Gly Leu Arg Ala Lys Arg Ile Pro
4385 4390 4395 4400

Val Asp Tyr Ala Ser His Cys Pro His Val Gln Pro Leu His Asp Glu
4405 4410 4415

Leu Leu His Leu Leu Gly Asp Ile Thr Pro Gln Pro Ser Thr Met Pro
4420 4425 4430

Phe Phe Ser Thr Val Val Gly His Leu Val Trp Tyr Thr Thr Thr Leu
4435 4440 4445

Asp Ala Ala Tyr Trp Tyr Arg Asn Leu His Gln Pro Val Arg Phe Ser
4450 4455 4460

His Ala Ile Gln Thr Leu Thr Asp Asp Gly His Arg Pro Phe Ile Glu
4465 4470 4475 4480

Ile Ser Pro His Pro Thr Leu Val Pro Ala Ile Glu Asp Thr Thr Glu
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Asn Thr Thr Glu Asn Ile Thr Ala Thr Gly Ser Leu Arg Arg Gly Asp
4500 4505 4510

Asn Asp Thr His Arg Phe Leu Thr Ala Leu Ala His Thr His Thr Thr
4515 4520 4525

Gly Ile Arg Thr Pro Thr Thr Trp His His His Tyr Thr Gln Thr His
4530 4535 4540

Pro His Pro His Asn His His Leu Asp Leu Pro Thr Tyr Pro Phe Gln

4545

4550

4555

4560

His Gln His Tyr Trp Leu Gln Pro Pro Thr Thr Thr Thr Asp Leu Thr

4565

4570

4575

Thr Thr Gly Leu Thr Pro Thr His His Pro Leu Leu Thr Ala Thr Leu

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4585

4590

Thr Leu Ala Asn Asn Asn Thr Gln Leu Leu Thr Gly Arg Leu Ser Leu

4595

4600

4605

Arg Thr His Pro Trp Leu Thr Asp His Thr Val Val Gly Thr Thr Leu

4610

4615

4620

Val Pro Gly Thr Ala Leu Leu Glu Leu Ala Leu Gln Ala Thr Thr Thr

4625

4630

4635

4640

Asp His Leu Glu Glu Leu Ala Leu His Thr Pro Leu Val Ile Pro Arg

4645

4650

4655

Glu Gly Ala Val Asp Val Gln Val His Ile Asn Pro Pro Asp Asp Thr

4660

4665

4670

Asp Thr Arg Ser Leu Thr Ile Tyr Ser Arg Ser Glu Asn Ala Pro Ala

4675

4680

4685

Ala Ala Pro Trp Arg His His Ala Thr Ala Val Leu Gly Thr Lys Thr

4690

4695

4700

Ser Arg Ile Glu Thr Gly Arg Ser His Asp Asp Leu Ser Met Trp Pro

4705

4710

4715

4720

Pro Ala Gly Ala Val Arg Cys Ala Asp Glu Glu Leu Ala Ala Leu Tyr

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4730

4735

Gly Asp Tyr Glu Ala Asn Gly Phe Val Tyr Gly Pro Ala Phe Arg Gly

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4745

4750

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Leu Thr Ala Ala Trp Arg Leu Gly Asp Glu Val Phe Ala Glu Val Arg
4755 4760 4765

Leu Pro Glu Gln Val His Gly Glu Ala Ser Ala Tyr Asn Leu His Pro
4770 4775 4780

Ala Leu Leu Asp Ala Ala Leu His Ala Ala Ala Phe Ala Pro Ser Gly
4785 4790 4795 4800

Ser Leu Pro Gln Gly Ser Val Pro Phe Ser Phe Thr Gly Val Thr Leu
4805 4810 4815

His Ala Ala Asn Ala Ser Ser Leu Arg Val Arg Leu Ser Pro Ala Asp
4820 4825 4830

Pro Asn Ser Gly His Ala Ala Val Ser Val Leu Val Thr Asp Asp Thr
4835 4840 4845

Gly Thr Pro Val Ala Ser Val Glu Ala Leu Ala Val Arg Pro Leu Ala
4850 4855 4860

Ala Asp Glu Leu Arg Ala Ala Glu Arg Ala Val Gln Arg Ala Glu Leu
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Phe Asp Met Lys Trp Val Glu Val Pro Ser Asp Val Leu Val Ser Gly
4885 4890 4895

Gly Ala Ser Val Val Val Leu Asp Gly Ala Asp Asp Leu Val Gly Leu
4900 4905 4910

Ala Ala Glu Glu Asp Gly Val Pro Gly Val Val Val Leu Arg Cys Pro
4915 4920 4925

Asp Ala Gly Ala Asp Gly Gly Gly Gly Gly Gly Gly Val Gly Glu Val
4930 4935 4940

Val Gly Gly Val Leu Gly Val Val Gln Gly Trp Leu Gly Leu Glu Arg
4945 4950 4955 4960

5155

5160

5165

Val Val His Ala Ala Gly Val Leu Asp Asp Ala Thr Ile Ala Ser Leu

5170

5175

5180

Thr Pro Glu Arg Leu Gly Thr Val Phe Ala Ala Lys Val Asp Ala Ala

5185

5190

5195

5200

Leu Leu Leu Asp Glu Leu Thr Arg Gly Met Glu Leu Ser Ala Phe Val

5205

5210

5215

Leu Phe Ser Ser Ala Ala Gly Ile Leu Gly Ser Ala Gly Gln Gly Asn

5220

5225

5230

Tyr Ala Ala Ala Asn Ala Ala Leu Asp Ala Leu Ala Tyr Arg Arg Arg

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5240

5245

Ala Ala Gly Leu Pro Gly Val Ser Leu Ala Trp Gly Leu Trp Glu Glu

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5255

5260

Ala Ser Gly Met Thr Gly His Leu Ala Gly Thr Asp His Arg Arg Ile

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5270

5275

5280

Ile Arg Ser Gly Leu His Pro Met Ser Thr Pro Asp Ala Leu Ala Leu

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5290

5295

Phe Asp Ala Ala Leu Ala Leu Asp Arg Pro Val Leu Leu Pro Ala Asp

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5310

Leu Arg Pro Ala Pro Pro Leu Pro Pro Leu Leu Gln Asp Leu Leu Pro

5315

5320

5325

Ala Thr Arg Arg Arg Thr Thr Arg Thr Thr Thr Thr Gly Gly Ala Asp

5330

5335

5340

Asn Gly Ala Gln Leu His Gly Arg Leu Ala Gly Gln Thr His Glu Gln

5345

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5355

5360

Gln His Thr Thr Leu Leu Ala Leu Val Arg Ser His Ile Ala Thr Val
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Leu Gly His Thr Thr Pro Asp Thr Ile Pro Pro Asp Arg Ala Phe Arg
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Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu Arg Asn Arg Leu
5395 5400 5405

Ser His Thr Thr Gly Leu Arg Leu Pro Thr Thr Leu Ala Phe Asp His
5410 5415 5420

Pro Asn Pro Thr Thr Leu Thr His His Leu His Thr Gln Leu Val Ser
5425 5430 5435 5440

Lys Gly Leu Thr Ala Ala Ala Glu Pro Asp Ala Ala Thr Thr Pro Pro
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Gly Leu Pro Ser Leu Leu Ser Glu Leu Glu Arg Leu Glu Ala Val Val
5460 5465 5470

Leu Ser Ser Thr Thr Ser Ser Ala Ala Pro Leu Asp Asp Gly Ala Arg
5475 5480 5485

Thr Arg Leu Ala Ser Arg Leu His Ser Leu Ala Gln Lys Leu Asn Gly
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Asp Asp Thr Ala Pro Asp Leu Ala Glu Thr Ser Asp Glu Glu Met Phe
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Ala Leu Ile Asp Arg Glu Val Gly Phe Glu Ser Gln
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<212> DNA

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gga ctc gac ccc acc gaa cac ccc cta ctc ggc gcc aca ttg gaa ctg 96
Gly Leu Asp Pro Thr Glu His Pro Leu Leu Gly Ala Thr Leu Glu Leu
20 25 30

gcg act gac ggt gga gcg ctt ctt gca ggg cgc ttg tct ttg agg tcg 144
Ala Thr Asp Gly Gly Ala Leu Leu Ala Gly Arg Leu Ser Leu Arg Ser
35 40 45

cat ccg tgg ctg gct gac tac gag gtc ggc ggc acg gtg ctg ctg tcg 192
His Pro Trp Leu Ala Asp Tyr Glu Val Gly Gly Thr Val Leu Leu Ser
50 55 60

ggc gcc acc ttc ctc gaa ctc gcc ctt cat gcg ggc aca tac gtg ggc 240
Gly Ala Thr Phe Leu Glu Leu Ala Leu His Ala Gly Thr Tyr Val Gly
65 70 75 80

tgc gac cga gtg gat gag ctg acg ctg cat gcg ccg ctg gtg gtt cct 288
Cys Asp Arg Val Asp Glu Leu Thr Leu His Ala Pro Leu Val Val Pro
85 90 95

gtg gat ggg ggt gtg agt gtg cag gtt ggg gtt gcg gct gcg gat ggg 336
Val Asp Gly Gly Val Ser Val Gln Val Gly Val Ala Ala Ala Asp Gly
100 105 110

gag ggg cgg cgt ttg gtg agt gtg tat gcg cgg ggt ggg agt gct tgt 384
Glu Gly Arg Arg Leu Val Ser Val Tyr Ala Arg Gly Gly Ser Ala Cys
115 120 125

ggt ggg ggt ggt gcg tcg ggt ggg gtg tgg acg tgt cat gcc tcg ggg 432
 Gly Gly Gly Gly Ala Ser Gly Gly Val Trp Thr Cys His Ala Ser Gly
 130 135 140

gtg ctg 438
 Val Leu
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<210> 8
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 <212> PRT
 <213> Streptomyces avermitilis

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Ala Thr Asp Gly Gly Ala Leu Leu Ala Gly Arg Leu Ser Leu Arg Ser
 35 40 45

His Pro Trp Leu Ala Asp Tyr Glu Val Gly Gly Thr Val Leu Leu Ser
 50 55 60

Gly Ala Thr Phe Leu Glu Leu Ala Leu His Ala Gly Thr Tyr Val Gly
 65 70 75 80

Cys Asp Arg Val Asp Glu Leu Thr Leu His Ala Pro Leu Val Val Pro
 85 90 95

Val Asp Gly Gly Val Ser Val Gln Val Gly Val Ala Ala Ala Asp Gly
 100 105 110

Glu Gly Arg Arg Leu Val Ser Val Tyr Ala Arg Gly Gly Ser Ala Cys
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Gly Gly Gly Gly Ala Ser Gly Gly Val Trp Thr Cys His Ala Ser Gly
 130 135 140

Val Leu
 145

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 <212> DNA
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<220>
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 of SEQ ID NO:1.

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 <213> Artificial Sequence

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 9193 and 9222 of SEQ ID NO:1.

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 <212> DNA
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09914386-082404

<220>

<223> Designated is an antisense primer based on the sequence between 9098 and 9127 of SEQ ID NO:1.

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<211> 10

<212> PRT

<213> Streptomyces avermitilis

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<223> Xaa denotes an unspecified amino acid.

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<211> 10

<212> PRT

<213> Streptomyces avermitilis

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<211> 10

<212> PRT

<213> Streptomyces avermitilis

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<400> 15

Tyr Xaa Xaa Xaa Gly Xaa Xaa Xaa Xaa Ser

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<210> 16

<211> 10

<212> PRT

<213> Streptomyces avermitilis

<400> 16

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